COUNTWAY LIBRARY
HC 4VWS

3.76.167.

BOSTON MEDICAL LIBRARY

PURCHASED FROM THE INCOME OF THE

OLIVER F. WADSWORTH FUND

A Course in Normal Histology

By Professor Rudolf Krause, Berlin. Translation by Philip J. R. Schmahl, M.D., New York. A Course in Normal Histology. A Guide for Practical Instruction in Histology and Microscopic Anatomy. With 30 Illustrations in the Text and 208 Colored Pictures, Arranged on 98 Plates, After the Original Drawings by the Author. *Part I, 96 pages, Cloth, 75 Cents. Part II, 416 pages, Cloth, $5.50.*

CONTENTS

Part I.—The Microscope—Rules for the Use of the Microscope—General Microtechnique Methods—Methods of Preservation—Preparation of Sections—Staining Methods—Impregnation Methods—Methods of Injection—Mounting and Finishing—Mensuration and Drawing.

Part II.—I. The Cell—II. The Tissues of the Animal Body—1. Epithelium—2. Connective Tissue—3. Cartilage—4. Bone—5. Muscle—6. Nerve Tissue—7. Blood—III. Organs—7. Circulatory Organs—2. Glands—3. Organs of Digestion—4. Organs of Respiration—5. Urinary and Genital Organs—6. Organs of Motion—7. Organs of the Nervous System—8. Organs and Sense—9. The Skin—Index.

ABSTRACTS FROM REVIEWS

"The illustrations are excellent and well chosen; the descriptions are clear and concise. . . ."—*Johns Hopkins Hosp. Bulletin.*

"This is the most comprehensive work on histology, and one every one should possess. . . ."—*Wisconsin Med. Recorder.*

"An abundance of text-books exists on the subject of histology, some of them having been standards for many years, but no more beautifully illustrated volume than this has appeared at so low a price. . . ."—*Medical Record (N. Y.)*

"This is a collection of two hundred and eight superb histological plates of tissues and organs with their brilliant stains, all presented with a care and degree of perfection seldom equalled in works available to the student."—*New York Med. Jl.*

"The publications of the Rebman Company excel in respect of illustration, and this one is no exception. A student who owned this handsome volume might well consider himself fortunate."—*Canadian Med. Assoc. Jl.*

"This is the finest series of colored plates, both microscopic and gross, as yet presented for study. The Rebman Company in the last ten years has given a great boost to medical science in the United States by their masterly array of French, German and Italian authorities, lavishly illustrated and indispensable to anatomy, pathology and differential diagnosis. The device of their trademark on every volume, "Age quod agis" (Do what thou doest), should be an inspiration to the student as it has been to the publishers in putting before us those fundamental works such as the present treatise. They have stability and permanent value. . . ."—*Indianapolis Med. Jl.*

"We might cast our superlatives not only at Krause, but also at Schmahl (the translator), at Rebman (the publisher) and at the art printers. We hope that our American schools will adopt this work for practical histology and leave the theory to the lecturer. . . ."—*Archives of Diagnosis.*

"Krause's teachings are beginning to have effect in the English-speaking countries, and doubtless by the translation of his book more rapid strides will be made in bringing histology into its own. . . ."—*Maryland Med. Jl.*

"Rebman Company is giving us an excellent series of scientific text-books translated from European texts, of which this is one of the best examples. It is fitting that a teaching book on Histology should excel in its illustrations, since it is only through the visual faculty that histology can be properly imparted and acquired. And this book does excel in its illustrations, containing as it does some of the finest pictorial representations of tissue-structures that it has ever been our pleasure to see."—*Clinical Medicine.*

"The work is written from the modern standpoint and is especially to be commended for its practical character."—*Interstate Med. Jl.*

"To teachers and students alike it will prove acceptable as a proper guide in Histology."—*Dominion Med. Monthly.*

"This work—as would be expected at the hands of such a man—covers the ground clearly and tersely, not only as to text, but by arrangement and type. . . ."—*Jl. of Ophthalmology, Otology and Laryngology.*

"To one even slightly familiar with histology as a subject, the work has hardly an equal as a reference book."—*New Orleans Med. and Surg. Jl.*

"The plates are most excellent and leave nothing to be desired."—*Canadian Practitioner and Review.*

PUBLISHER'S ANNOUNCEMENT

The Plates and Figures quoted in the pages of "A Textbook of Histology" refer to the Plates and Figures contained in R. Krause's "A Course in Normal Histology," and are cited by the author for the purposes of illuminating his lectures.

We offer this work to teachers and students alike as a guide in Histology. Professor *Krause* strikes a keynote in his preface to the book. The study of Histology should go hand in hand with that of Anatomy. The one cannot be separated from the other nowadays without serious injury to the student.

The reason why we publish this work in two parts is apparent.

The ***First Part*** is simply a guide to the technique of Microscopy and may be used by students of medicine as well as by those who pursue subjects of science foreign to medicine.

The ***Second Part*** deals exclusively with Histology and therefore appeals chiefly to the medical man.

The author's aim is to place at the disposal of the student a book of reference which is both practical and theoretical, as well as to furnish the teacher with a textbook that will serve as a detailed, clear, concise and methodical guide through the course of Microscopy and Histology.

So far as the student of medicine is concerned he will in the first part find much valuable information appertaining to the microtechnique with which the student of pathology must needs be familiar.

The subject of microtechnique is in most all of the English written books on this topic treated but briefly. *Krause's* work not only acquaints the student in a thorough fashion with the theory and manipulation of the microscope, but introduces him also to ***all the methods*** employed in preparing a specimen for microscopic examination from start to finish.

Professor *Krause* justly attaches great importance to the matter of drawing the specimens from the microscope. The illustrations in the second part are true reproductions of the colored drawings made by the author himself, and are intended not only to illuminate the text matter, but also to stimulate the student to practical efforts in reproducing on paper his own microscopical findings. (*See preceding page.*)

F. J. Rebman, *Pres.*

REBMAN COMPANY.

New York, 141, 143, 145 West 36th Street.

A TEXTBOOK

OF

HISTOLOGY

BY

RUDOLF KRAUSE

A. O. PROFESSOR OF ANATOMY AT THE UNIVERSITY OF BERLIN

TRANSLATED FROM AN ORIGINAL MANUSCRIPT AND PRINTED ONLY IN THE ENGLISH LANGUAGE

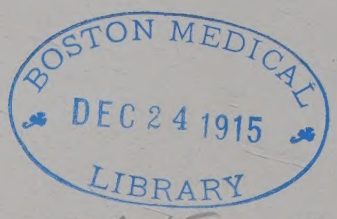
WITH THIRTY-SIX ILLUSTRATIONS IN THE TEXT, THREE OF WHICH ARE COLORED

THE REFERENCES TO ILLUSTRATIONS GIVEN IN THE TEXT RELATE TO THE COLORED ILLUSTRATIONS CONTAINED AND PUBLISHED IN DR. RUDOLF KRAUSE'S "A COURSE IN NORMAL HISTOLOGY"

NEW YORK

REBMAN COMPANY

141, 143 AND 145 WEST 36TH STREET



13206 Wad 2.25

COPYRIGHT, 1915, BY
REBMAN COMPANY
NEW YORK

All Rights reserved

PRINTED IN AMERICA

INTRODUCTION

The bodies of all of the higher animals, including man, are composed of a large number of single **organs,** with a distinct function allotted to each in the general economy. To give a simple example: The kidney is the organ of the human body to which is entrusted the duty of excreting the end products formed elsewhere by metabolism. The ureter, bladder, and urethra are supplementary organs attached to it to provide means for the final elimination of its product from the body, and we call any such interrelated group a **system of organs.**

In order to fulfill its own special duty each organ has its own peculiar structure, which is fixed and unchangeable under normal conditions; i.e., it is constructed of certain **tissues** arranged in a definite manner. The same tissues are met with in almost every organ, but their arrangement in each is quite typical.

Organs are composed of epithelial, supporting, muscular and nervous tissues. These are not the primary components of the human body, but each is made up of minute, elementary particles, called **cells,** with an **intermediate substance** derived from these cells in many cases. Cells are therefore the real elements of the human body, and every description of its minute structure must begin with and be based upon them. Hence the investigation of all of the material composing the microscopic anatomy of the human body falls naturally into three large sections:

I. The cell.

II. The tissues.

III. The structure of the individual organs.

TABLE OF CONTENTS

PAGE

INTRODUCTION iii

PUBLISHERS' ANNOUNCEMENT iv

A. THE CELL 1

Form and Size of Cells 1
Construction of the Cell 2
The Cell Body 2
The Nucleus 4
The Central Bodies 6
The Chondriosomes 7
The Reticular Apparatus 7
The Biological Properties of the Individual Constituents of the Cell . . 7
The Manifestations of Life in the Cell 8
The Metabolism of the Cell 8
Reaction of the Cell to External Stimuli 10
The Propagation of the Cell 11
Indirect Segmentation 12
Direct Segmentation 15

B. THE TISSUES 16

EPITHELIAL TISSUE 17
Simple Epithelium 20
Stratified Epithelium 21
Stratiform Epithelium 23
Glandular Epithelium and Glands 24
The True Glands 25
Closed and Solid Glands 29

MUSCULAR TISSUE 32
Smooth Muscular Tissue 32
Striated Muscular Tissue 33
The Cardiac Muscle Fiber 38
Nervous Tissue 39
Nerve Cells 41
The Nerve Fiber 45
Glia Tissue 47
The Development of Nervous Tissue 48
The Supporting Tissue 49
The Chordal Tissue 50
The Vesicular Supporting Tissue 50
The Gelatinous Tissue 51

B. THE TISSUES—*Continued*

Muscular Tissue PAGE
The Vitreous Tissue 51
The Reticular Tissue 51
The Neuroglia Tissue 52
The Connective Tissue 52
Cartilaginous Tissue 57
Hyaline Cartilage 58
Fibrocartilage 60
Elastic Cartilage 61
Osseous Tissue 61

C. MICROSCOPIC ANATOMY OF ORGANS 66

I. THE VASCULAR SYSTEM 66

1. The Blood 66

The Red Blood Corpuscles 67
The White Blood Corpuscles 68
The Blood Platelets 70
The Hæmokonia 71
Physiological Importance and Replacement of the Corpuscular Elements of the Blood in Adults 71

2. The Blood Vessels 72

The Capillaries 73
The Arteries 73
The Veins 75
The Vessels and Nerves of the Blood Vessels 76
3. The Heart 76
4. The Lymph 79
5. The Lymphatics 79
6. The Lymphoid Organs 80
7. The Spleen 82

II. THE DIGESTIVE ORGANS 84

1. The Lips 84
2. The Teeth 86
a. The Dentine 88
b. The Enamel 89
c. The Cement 89
d. The Dental Pulp 90
e. The Periodontal Membrane 90
f. The Gums 90
3. The Tongue 91
4. The Palate 94
5. The Salivary Glands 95
The Submaxillary Gland 96
The Sublingual Gland 98
The Parotid Gland 98

C. MICROSCOPIC ANATOMY OF ORGANS—*Continued*

II. THE DIGESTIVE ORGANS

PAGE

6. The Pharynx 99
7. The Œsophagus 100
8. The Stomach 101
9. The Intestine 105
The Liver 111
The Gall Bladder 115
The Pancreas 116
The Peritoneum 119

III. THE RESPIRATORY ORGANS 121

1. The Nasal Cavity 121
2. The Larynx 123
3. The Trachea and the Extrapulmonary Bronchi 125
4. The Lungs and the Intrapulmonary Bronchi 126
5. The Pleura 129
6. The Diaphragm 130
7. The Thyroid Gland 131
8. The Parathyroids 132
9. The Thymus 133

IV. THE URINARY ORGANS 136

1. The Kidney 136
2. The Pelvis of the Kidney and the Ureter 144
3. The Urinary Bladder 145
4. The Urethra 146
a. The Male Urethra 147
b. The Female Urethra 148
5. The Suprarenal Capsules 149
6. The Carotid Gland 151
7. The Glomus Coccygeum 151

V. THE MALE SEXUAL ORGANS 152

1. The Testicles 152
2. The Excretory Passages of the Testicles 156
a. The Epididymis 156
b. The Vas Deferens 156
c. The Seminal Vesicles 157
d. The Ejaculatory Ducts 157
e. The Prostate 157
f. Cowper's Glands 159
g. The Semen 159
h. The Penis 162

VI. THE FEMALE GENITAL ORGANS 165

1. The Ovary 165
2. The Fallopian Tube 170
3. The Uterus 171

C. MICROSCOPIC ANATOMY OF ORGANS—*Continued*

VI. THE FEMALE GENITAL ORGANS

PAGE

4. The Vagina 174
5. The External Female Genital Organs 176
   a. The Vestibule of the Vagina 176
   b. The Clitoris 176
   c. The Labia Minora 176
   d. The Labia Majora 177

VII. THE ORGANS OF MOVEMENT 178

1. The Muscles 178
2. The Tendons 180
3. The Bones 181
4. The Joints 183
5. The Synarthroses 184

VIII. THE ORGANS OF THE NERVOUS SYSTEM 185

1. The Spinal Cord 185
   a. The Gray Matter 188
   b. The White Matter 190
   c. The Anterior Roots 192
   d. The Posterior Roots 192
   e. The Neuroglia of the Spinal Cord and the Central Canal . . 193
   f. The Blood Vessels of the Spinal Cord 194
   g. The Lymphatics of the Spinal Cord 195
2. The Spinal Ganglia 195
3. The Brain 197
   a. The Nuclei of the Afterbrain and Midbrain 197
   b. The Cortex of the Cerebellum 201
   c. The Nuclei of the Cerebellum 203
   d. The Nuclei of the Midbrain and Interbrain 203
   e. The Hypophysis 205
   f. The Epiphysis 206
   g. The Cerebral Cortex 207
   h. The Olfactory Bulb 209
4. The Membranes of the Central Nervous System 210
5. The Cerebral Ganglia 211
6. The Sympathetic Ganglia 211
7. The Peripheral Nerves 212

IX. THE ORGANS OF SENSE 214

1. The Eye 214
   a. The Retina 214
   b. The Optic Nerve 220
   c. The Choroid 221
   d. The Ciliary Body 222
   e. The Iris 224
   f. The Lens 225
   g. The Cornea 227

C. MICROSCOPIC ANATOMY OF ORGANS—*Continued*

IX. THE ORGANS OF SENSE

PAGE

h. The Sclera 229
i. The Vitreous 230
k. The Zonula Ciliaris 230
l. The Blood Vessels of the Eyeball 231
m. The Lymphatics of the Eyeball 232
n. The Nerves of the Eyeball 233
o. The Eyelids and the Conjunctiva 233
p. The Lacrimal Glands 236
q. The Lacrimal Passages 237
r. The Extrinsic Ocular Muscles 237

2. The Ear 238
a. The Internal Ear 238
b. The Middle Ear 245
c. The External Ear 247
3. The Olfactory Organ 249
4. The Organ of Taste 250

X. THE SKIN 252

The Hair 255
The Nails 257
The Sweat Glands 258
The Sebaceous Glands 259
The Blood Vessels of the Skin 260
The Lymphatics of the Skin 260
The Nerves of the Skin 260
The Mammary Gland 262

LIST OF ILLUSTRATIONS

FIG. PAGE

1—Structure of a Cell 2

2—Indirect Segmentation of the Nucleus (*Stage of the Spirem*) 12

3—Indirect Segmentation of the Nucleus (*Stage of the Formation of the Pole-field*) 12

4—Indirect Segmentation of the Nucleus (*Stage of the Monaster*) 13

5—Indirect Segmentation of the Nucleus (*Barrel Stage*) 14

6—Indirect Segmentation of the Nucleus (*Stage of the Daughter Spirem*) . . 14

7—Ciliated Cell 17

8—Simple Flat Epithelium (*Schematic*) 20

9—Simple Cuboidal Epithelium with Intercellular Spaces and Cement Wedges (*Schematic*) 20

10—Simple Cylindrical Epithelium with Intercellular Spaces and Cement Wedges (*Schematic*) 21

11—Stratified Flat Epithelium with Intercellular Spaces and Intercellular Bridges (*Schematic*) 22

12—Transitional Epithelium (*Schematic*) 22

13—Stratified Cylindrical Epithelium (*Schematic*) 23

14—Stratiform Epithelium (*Schematic*) 23

15—Sensory Epithelium of the Membranous Labyrinth of the Ear (*Schematic*) 24

16—Simple Tubular Gland (*Schematic*) 25

17—Sweat Gland (*Schematic*) 26

18—Simple Branched Tubular Gland (*Schematic*) 26

19—Compound Branched Tubular Gland (*Schematic*) 26

20—Simple Alveolar Gland (*Schematic*) 27

21—Simple Branched Alveolar Gland (*Schematic*) 27

22—Compound Branched Alveolar Gland (*Schematic*) 27

23—Simple Alveotubular Gland (*Schematic*) 28

24—Branched Alveotubular Gland (*Schematic*) 28

25—Compound Branched Alveotubular Gland (*Schematic*) 29

FIG. PAGE

26—Transverse Striation of a Muscular Fibril 35

27—Schematic Representation of a Motor Neuron 40

28—Motor Nerve Cell of the Spinal Cord (*Semischematic*) 43

29—Schematic Picture of the Structure of a Lymphatic Gland 81

30—Schematic Picture of the Structure of the Spleen (*In 3 Colors*) . . . 82

31—Structure of the Liver (*In 3 Colors*) 112

32—Renal Canaliculi (*After Peter*) 138

33—The Divisions of the Blood Vessels in the Human Kidney (*Schematic*) (*In 3 Colors*) 144

34—Human Spermatozoon (*After Maves*) 160

35—Shapes and Sections of the Spinal Cord at Various Levels 187

36—The Columns of the White Matter of the Spinal Cord at the Level of the Fifth Cervical Nerves 190

BOSTON MEDICAL
DEC 24 1915
LIBRARY

A

THE CELL

We understand by a cell the final, elementary particle of any living organism which is able to live independently under certain circumstances. A large class of very low organisms, the protozoa, are nothing else than living single cells, and we learn from embryology that all other animals, even the most highly organized, come from a single cell, the ovum, or from the union of the ovum with the seminal cell. The union of the ovum with the seminal cell is the beginning of the fecundated egg, which finally produces the complete organism by continuous segmentation. Therefore we must remember, when we speak of the cell as the element, or the elementary organism of the human body, that this name is not given it because of the simplicity of its structure, it has, on the contrary, a very complicated structure which is as yet only partially understood. It is not an elementary particle in a chemical sense, it is only a biological unit. None of its parts can exist continuously without the others; the union of all is necessary to the life of an elementary particle.

Form and Size of Cells

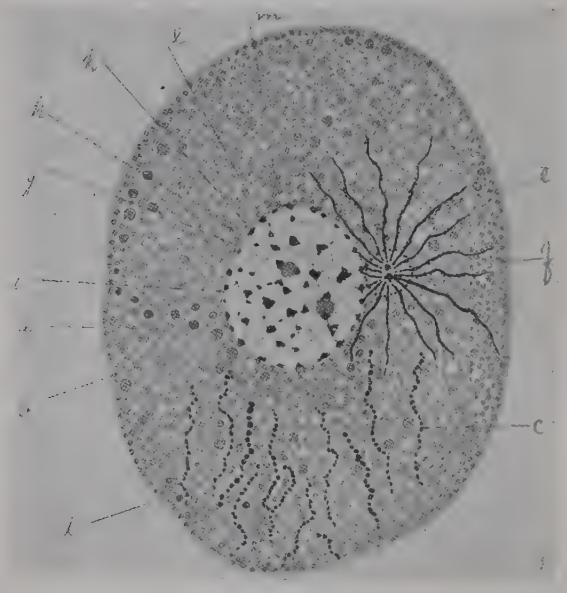
The fundamental form of an animal cell is that of a sphere or of an ellipsoid, but this undergoes numberless modifications, chiefly due to the limitations of space. The cells that take part in the formation of tissue lie close together and adapt their shapes to the spaces in which they are confined, and thus become cylindrical, cuboidal, flat, spindle-shaped, or polyhedral. Another important factor in determining the shape of the cell is the function of the organ of which it forms a part; thus muscle cells become spindle-shaped, or threadlike, and nerve cells throw out numerous processes, with which they seek to join others like themselves, conformably to their functions. Finally many cells change their shapes in response to external or internal stimuli, and it happens frequently that a local movement of the cell may be brought about by such an active change of form.

Cells vary in size as well as shape. The great majority of those of the human body are too small to be seen with the naked eye, but the muscle cells, nerve cells, and ova are exceptions. The human ovum has a diameter of 200 μ, and can therefore be seen without artificial aid. The ova of many animals are incomparably larger; this is particularly true of birds, in which the yolk is an enormously enlarged cell.

Construction of the Cell

The classical morphological definition of a cell given first by *Max Schultze* in 1861 is: A bit of protoplasm with a nucleus within it. Even now, after the lapse of more than fifty years, this definition has changed very little. The **cell body** and the **nucleus** are the most important constituents. The cell cannot last continuously without a nucleus, and free nuclei, without enveloping cell bodies, are just as little to be met with.

In the course of these fifty years we have learned, however, to recognize that there are other essential constituents pertaining to the cell, including the



a, protoplasm, consisting of hyaloplasm and granoplasm; *b*, paraplasm; *c*, mitochondria; *d*, ectoplasm; *e*, archoplasmic rays; *f*, central bodies; *g*, nuclear framework (linin); *h*, achromatic nuclear membrane; *i*, nuclear chromatin; *k*, chromatic nuclear membrane; *l*, nucleoli; *m*, nuclear juice.

Fig. 1.—Structure of a Cell.

membrane formations, the **central bodies,** the **reticular apparatus,** and the **chondriosomes,** or **mitochondria.** We will discuss each of these constituents in turn, beginning with the cell body.

The Cell Body

The body of the living cell is of a gelatinous or semisolid consistence, and is originally colorless, transparent, and weakly refractive. When it appears to be colored it is because of the presence of special pigment, or of fatty substances.

The main part of the cell body is composed of **protoplasm.** This is not chemically uniform, but is made up of a mixture of nucleoalbumins, proteids, globulins, and traces of albumins. Its composition probably varies in different kinds of cells. It is always alkaline, insoluble in water, and coagulable by the precipitants of albumin—heat, alcohol, mineral acids, and the salts of the heavy metals.

In many living cells the body appears to be homogeneous and structureless, but in others a structure can be discerned more or less clearly. If we kill a cell in a suitable manner the structure of its body stands out more distinctly, and we can recognize that it varies in different cells.

Very often the cell body presents the picture of an alveolar structure (Pl. 1, Figs. 1 and 2), i.e., the protoplasm forms partitions that pass through the body from the periphery to the nucleus and unite to form more or less regular alveoli. The individual alveoli may be completely separate from one another, or they may communicate, as they do in many cases. Granules appear to be deposited at the points where the walls of the alveoli meet, and, by using the highest magnifying power, we find that such granules are to be seen everywhere in the walls of the alveoli. These are the **microsomes** of the protoplasm, or the **plasmosomes,** and we speak of this framework and the granules together as the **granoplasm,** to distinguish it from the structureless part of the protoplasm, which we call the **hyaloplasm.** Sometimes nothing can be seen of an alveolar structure in the cell body, but the latter contains threads, or **fibrils,** running through the hyaloplasm, and then we say that the cell body has a fibrillary structure (Pl. 2, Fig. 6). These protoplasmic threads may constitute quite definite structures, as in the muscles, nerves, and many epithelial cells, and are then connected closely with the function of the cell, inasmuch as the body has assumed a fixed, stable formation fitted for the performance of its function, but in many other cases a fibrillary structure of the protoplasm is not of so great consequence. In such cases the fibrils are not arranged so typically, but run more irregularly, interlace, cross one another, or form true networks in the cell body. We call these threadlike constituents embedded in the hyaloplasm the **cytomitome.** Wherever the formation of a cytomitome has taken place we always find with it in the hyaloplasm larger or smaller microsomes, and it is quite possible that the fibrils of the cytomitome, which often present swellings that make them look like strings of pearls, are produced by the lining up one after another of numberless minute microsomes. In that case the cytomitome is simply a certain phase of the granoplasm.

Very often the greater part of the cell body appears to be granular, and then we speak of a ***granular*** protoplasm. Such an appearance may be due to the presence of many large microsomes in an otherwise hyaline protoplasm, but it may also be simulated in a cell body of alveolar structure when the alveoli are filled with some substance that makes itself prominent.

In addition to protoplasm the cell body very often contains another substance, known as the **paraplasm,** or the **deutoplasm,** which fills the interspaces left open by the protoplasm between the alveoli. This may be fluid or solid. In the majority of cases it is formed of materials that owe their presence to the activity of the protoplasm itself, or have been taken up from outside into the cell body. Glycogen is found very extensively as a deutoplasmatic constituent of cells in the form of fine granules, or of coarse flakes in the retiform spaces of the protoplasm (Pl. 3, Fig. 7). Fat enjoys an equally wide distribution, appearing in minute particles which, when in great numbers, often fill the cell body, and may blend into large drops (Pl. 3,

Fig. 9). Other substances met with are mucus and its rudiments, lipoids, enzymes, and the vitelli of embryonal cells.

Externally the protoplasm becomes condensed and excludes the cell body from the outer world as by a membrane, but this so-called cell membrane is nothing else than protoplasm, and must not be confused with the membrane of the plant cell, which consists of cellulose and differs both chemically and morphologically from the cell protoplasm. It is better therefore not to call it a membrane, but to speak of it as an **ectoplasm,** or a **crusta.**

The Nucleus

There is only one exception to the rule that a nucleus is to be found in every cell—it cannot be seen in the erythrocytes, the red blood corpuscles of man and the mammals. These cells are nucleated at first, but the nucleus gradually becomes invisible as they take up the coloring matter of the blood, the hæmoglobin. It has not yet been determined with certainty whether the nucleus becomes extruded from the cell, dies, or is simply hidden.

The great majority of cells contain only one nucleus apiece, yet there are varieties in which two nuclei are to be seen very often, like those of the liver. Polynucleated cells are comparatively rare in man under normal conditions, though they are much more common in the lower animals. The human red bone marrow contains polynucleated cells, which have also been called giant cells on account of their size (Pl. 2, Fig. 6); and the osteoclasts, which, as we shall see later, play an important part in the development of the medullary cavities of the bones, are likewise polynucleated. Such cells appear far more often in pathological conditions, such as rapidly growing tumors, like carcinomata, or tuberculous or syphilitic neoplasms, when more than a hundred nuclei may be found in a cell.

The size of the nucleus is usually proportionate to that of the cell body, so that we may say as a general rule that the larger the body the larger the nucleus, but there are many exceptions to this rule. In certain blood cells, the lymphocytes, the body is so small as to form only a narrow ring about the nucleus. The size of the nucleus also fluctuates considerably during the life of many cells, as in the ovum. In the glandular cells the nucleus may be greatly reduced in size and deformed by the pressure of the deutoplasmatic substances produced or stored away in the cell body.

The shape of the nucleus is even more variable than its number or size, and is very often influenced greatly by that of the cell body. Its fundamental form is spherical. If the cell body elongates, the nucleus does likewise and changes from a sphere first into an ellipsoid, and finally into a cylindrical or spindle shape. Very often spherical nuclei are to be seen that seem to be indented at a certain place (Pl. 2, Fig. 4). The indentation may be so deep as to break through into the center of the nucleus and to convert the sphere into a ring. Annular nuclei may be of uniform thickness everywhere, or they may have nodules in places that cause them to resemble rosaries, or rings of pearls. Nuclei that are shaped like horseshoes, or are lobulated, are not uncommon (Pl. 2, Fig. 5). The neutrophilic leucocytes and the eosinophilic

blood cells are particularly rich in such dissimilar forms of nuclei. In the bone marrow and the spleen of many mammals, such as rabbits, hedgehogs, and moles, we find cells that contain nuclei which have the form of spherical, fenestrated shells, and in which an intranuclear and an extranuclear cell body can be distinguished, connected by numerous bridges that break through the spherical shell (Pl. 2, Fig. 6). In cells that possess an active power of movement, like the lymphocytes of the blood, the form of the nucleus changes with the movement. That the nucleus has no fixed, unchangeable form may be seen very beautifully while watching the circulation in the frog, when the shape of the cell body and of the nucleus of the blood corpuscle will be observed to change greatly as it passes through narrow places, or enters lateral twigs.

The position of the nucleus within the cell varies a great deal. It is often central in the spherical nerve cell, while in the likewise spherical ovum it is almost always excentric. In cylindrical cells it lies sometimes in the middle, sometimes near the base, sometimes near the surface. Its location may be changed passively by the pressure of the adjacent cells, or by that of the deutoplasmatic contents of the cell itself, but many nuclei seem to possess a power of active movement. Distinct amœboid movements may be seen in the nucleus of the human ovum, the so-called germinal vesicle.

Turning now to the structure of the nucleus, if we stain a section of the human liver with hæmatoxylin the nuclei of the liver cells stand out as circular bodies bounded externally, toward the cell body, by a blue, irregular outline, and containing numerous more or less minute particles stained blue. This substance, thus brought into prominence by the ordinary stain of the nucleus, bears the name of **chromatin.** It is so distributed as to form an incomplete membrane about the nucleus, the ***chromatic membrane,*** and to appear within it in larger or smaller masses. If we would study the properties of this body more closely we must employ a more delicate method of staining. The best way is to treat the preparation with a mixture containing an acid and a basic coloring matter (Pl. 1, Figs. 1 and 2). The chromatin selects the basic color and becomes stained accordingly; we therefore say that chromatin is ***basophilic.*** The basophilia of chromatin depends on its content of nucleinic acid, an albuminoid rich in phosphorus, which forms the characteristic product of chemical decomposition, the so-called nuclein base. Only a very minute portion of this is free in the chromatin, the most of it is combined with other albumins to form the so-called nuclein. The amount of chromatin in the nucleus varies a great deal; often its particles can scarcely be seen (Pl. 1, Fig. 3), while in other cases they almost fill its entire interior (Pl. 1, Fig. 2).

If the chromatin contains only a little nucleinic acid it may cease to be basophilic and stain with the acid instead of the basic dye. We then speak of oxyphilic chromatin, which is found in the germinal vesicle of the ovum and in the nucleus of the nerve cell.

The nucleus contains in addition to chromatin a corpuscle, usually spherical, which is stained with hæmatoxylin; this we call the **nucleolus.** The nucleolus varies much in size and is quite large in some nuclei, as in the germinal vesicle of the ovum and in the nucleus of the nerve cell. It is by no

means rare for several to be present. Its position is inconstant; it may be central or excentric, but it is never in the chromatic membrane. When the preparation is stained with hæmatoxylin the nucleolus has the same color and intensity as chromatin, but when a mixture of acid and basic dyes is employed it behaves differently from chromatin in that it selects the acid stain, and thus proves itself to be oxyphilic (Pl. 1, Fig. 1). It is composed of pyronin, which differs from nuclein in containing little phosphorus.

The name **chromatic substance** is used to cover both the chromatin and the nucleolus, because they have a great affinity for coloring matters and may be stained very easily.

The nucleus contains in addition to the chromatic substance **achromatic substances,** which are more difficult to demonstrate. They are oxyphilic, i.e., they always select the acid dyes from a mixture, and are therefore similar in behavior to the cell protoplasm and the nucleolus. Two of these may be differentiated, the ***amphipyrenin*** and the ***linin.*** The former creates a membrane between the nucleus and the cell body, the **achromatic membrane,** while the linin forms a framework throughout the interior of the nucleus, the **achromatic framework.** The achromatic nuclear membrane is internal to the chromatin granules of the chromatic membrane, and the particles of chromatin have the same relation to the achromatic framework. The nucleolus, or nucleoli, is usually situated at the points of junction of this linin framework. All the meshes of this network are filled with the **nuclear fluid,** which is likewise achromatic and oxyphilic. A final constituent of the same nature is **lanthanin,** which appears in the form of little granules.

The Central Bodies

The central bodies, which are usually just visible with the microscope, were discovered by *Ed. v. Beneden* in 1876, and have been determined to be constant constituents of cells by very modern researches. They appear as two or more sharply defined granules usually lying close together in the cell body, never in the nucleus (Pl. 2, Figs. 4 and 5). As regards their position, all that can be said is that they have two places of predilection—the center and just beneath the free surface of the cell. The central position is characteristic of the colorless blood cells and of the cells of the smooth muscles, while the superficial is peculiar to the various epithelial cells (Pl. 8, Fig. 25).

They are generally two in number, and are frequently joined by a narrow bridge, a **centrodesmose.** Three central bodies occur in the nerve cells, the epithelial cells of the epididymis, and the cells of the lacrimal gland. Cells that deviate from the ordinary type in size vary with regard to the number of central bodies they may contain; as many as a hundred have been counted in the giant cells of the bone marrow (Pl. 2, Fig. 6).

The central bodies are oxyphilic, like protoplasm, yet many observations go to show that they are not of the same chemical composition.

They often form the center of a system of protoplasmic threads that radiate outward and are lost in the network of the cell protoplasm after a longer or shorter course (Pl. 2, Figs. 4 and 5). This radiating portion of the cell

protoplasm is called the **archoplasm.** The central bodies may also be surrounded by and lie in the center of a bright areola, through which the archoplasmic rays pass. At the margin of the areola each ray has a little thickening, a minute nodule, so that the central bodies seem to be within a sphere, which is called a **centrosphere,** while the entire structure is denominated a **centrosome.** Typical centrospheres are to be seen in the white blood cells and in the pigment cells, but chiefly in the ovum before and after impregnation, and in the segmentation cells, or blastomeres, of the impregnated ovum. In the majority of cases the central bodies have no centrosphere, but simply lie in a rather bright areola of protoplasm.

The Chondriosomes

The Chondriosomes, or mitochondria, are granules found in the protoplasm that stain differently from the microsomes. They were found first in ova and spermatozoa, but have now been demonstrated in almost all kinds of cells, and may be seen with beautiful distinctness in the cells of the embryonal body. As a rule they unite to form threads which run in wavy courses through the cell body (Pl. 3, Fig. 9, bf), or accumulate near the nucleus so as to form a sometimes spherical, sometimes crescentic body, known as the **accessory nucleus.**

The Reticular Apparatus

The final constituent of the cell is the reticular apparatus (Apparato reticolare), which was discovered by *Golgi* in the nerve cells, and has since been found in many others. In the most perfect cases it forms a network in the cell body about the nucleus, but in other varieties of cells it lies near the nucleus and envelopes the central bodies.

The Biological Properties of the Individual Constituents of the Cell

All important vital processes take place within the cell body, and particularly in its chief component, the protoplasm. We shall speak of this in another place. The question now arises of what importance the nucleus is to the cell. That it is of very great importance is proven by the fact that cells cannot continue to live without nuclei. This fact has been demonstrated experimentally many times; the nuclei have been removed from large cells, after which the cells live for a while, but soon die. The cell also loses with its nucleus its most important vital properties, and seems to retain only one, the power of movement. Infusoria deprived of their nuclei move just the same as normal ones, and the ciliated cells of the higher mammals continue to make regular strokes with their cilia after their nuclei have been removed. The nucleus has been thought by some to be the chief place of oxidation of the cell, but it seems to take no greater part in oxidation processes than the cell body. An important part in secretion has been ascribed to it, but without

cogent proof. Hence, although the activity of the nucleus is important to the life of the cell, it is apparently much less so than that of the cell body, while at the present time it is thought to be the most important, though perhaps not the sole bearer of the hereditary substances, which we have to seek in its chromatin.

The central bodies likewise are extremely important, as they play a determining part in the segmentation of the cell, as we shall see later.

The main activity of the mitochondria appears in embryonal life, when they are employed in the development of important differentiation products of the cell, but in postembryonal life the duty devolves upon them to produce certain constituents of secretion, as in the glandular cells.

Nothing positive is yet known concerning the physiological attributes of the reticular apparatus.

The Manifestations of Life in the Cell

Inasmuch as every organism is composed of cells, every manifestation of life must have to do with, originate from, and come to pass in these cells, and we may therefore say that every vital process, even when exhibited in so complicated an organism as the human body, consists of a great number of single processes, each of which takes place in a certain cell.

All of the manifestations of life that we are able to observe in animal bodies may be traced back to three elementary activities of the animal cells, thus:

1. The ability to admit into itself suitable foreign substances, to disintegrate them, to utilize them in its own construction, and to evacuate the products of elaboration. We call the phenomena that result from the exercise of this power **metabolism.**

2. The ability to receive energy from without in the form of stimuli and to transform it into heat, light, electricity, or mechanical energy, i.e., to transform it into change of form and movement.

3. The ability to propagate.

We will now discuss in some detail these three fundamental activities of the animal cell.

The Metabolism of the Cell

To repeat a comparison that has been made a great deal, each animal cell is a little chemical laboratory; it takes from its surroundings oxygen, water, and organic substances, supplies its own needs from them, and either eliminates the products of chemical decomposition, or forms from them simply constructed materials that are of service to the entire organism. The chemical processes that take place are extremely complicated. The fundamental difference between the cells of plants and of animals, and the importance of those of the former to those of the latter, are shown in the metabolism. The plant cell takes up simple inorganic substances in solution and transforms them by a wonderful process of synthesis into organic substances, carbohydrates, fat, and albumin. The carbohydrate, with its relatively simple molecule, is produced first, and from it is formed albumin with its highly complex molecule.

These organic bodies elaborated by the plant cell serve as nutriment to the animal cell, which has absolutely no other resource, as it cannot live on inorganic substances. The metabolism of the plant cell is a process of synthesis, that of the animal cell one of analysis, for it breaks up the complex bodies it admits into simpler ones.

Oxygen alone of the gases is of importance to the animal cell, while the plant cell may need carbon dioxide also. All animal cells without exception require oxygen, and cannot live without it. The taking up of oxygen by the cell we call ***respiration.***

The more highly differentiated are the cells in an organism the more sensitive they are to lack of oxygen. While the cells in a frog may live for hours without it, a few minutes of total deprivation suffice to kill human cells.

It was formerly thought that the processes of oxidation in the cell took place almost exclusively in the nucleus, and that this was the respiratory organ of the cell, but modern research has proved this idea to be erroneous, and that the nucleus and the cell body share equally in these processes. Cells without nuclei behave exactly the same as regards oxygen as those with nuclei. During the admission of oxygen highly organized bodies come into being in the cell, and are broken up again immediately with the production of carbon dioxide. This carbon dioxide is the end product of the gaseous changes in the animal cell and is thrown off by it as excrement, while it is assimilated by green plants under the influence of light, and is synthetized into a combination forming a more highly complex molecule, that of carbohydrate.

The principal fluid taken up by the animal cell is **water.** Life cannot last long where there is no water, for no organism can protect itself for any length of time against evaporation, and it is imperative that the evaporated water be replaced. Everything that the cell takes up and utilizes must be furnished it in a fluid form, so Nature has supplied the human body with a complete system of glands, the duty of which is to furnish secretions that render fluid the nutritive material introduced into the body, the greater part of which, including the albuminoids, the fat of meat, and the starch of cereals, is certainly insoluble in water.

Diffusion processes play a very considerable part in the entrance of water into the cell, but the living protoplasm is able to detain, in opposition to the current, the bodies dissolved in the fluid, and to select from among them the substances that it will permit to enter, and to reject those it does not want.

The elimination of the fluid products of metabolism is accomplished through an active contraction of the cell body. A diminution in the size of the latter may always be observed when this takes place. It may be that the nucleus also takes an active part in the process, for it has not only been observed to change its shape, but a protrusion of its constituents has been described as occurring in many processes of secretion.

The statement made above, that the animal cell can admit substances only when they are in solution, needs limitation in many respects. In the lowest, single-celled animal organisms, the protozoa, the cell, i.e., in these cases the organism itself, can admit solid bodies, render them fluid, and then assimilate them. With the aid of the microscope we can follow this process in these cells

in all its details. Either every part of the surface of the cell is fitted to receive the nutrient body, so that the latter is wrapped about by the cell body, and removed into it, or the cell has at a certain place a sort of mouth surrounded by cilia, through which the nutrient substance is passed into the cell body.

In the higher animals only a very few kinds of cells have this power of admitting corpuscular elements, and of these the lymphocytes of the blood are the most important. These cells have the power to move independently, and to press into all clefts in the tissue, so that there is hardly a place in the human body that is beyond their reach (Pl. 1, Fig. 3, wz). As they pass along they seize upon all of the fragments of cells and foreign substances they meet, and render them innocuous to the organism, thus taking an important part in the protection of the body against an invasion of foreign bodies.

Reaction of the Cell to External Stimuli

The animal cell possesses to a high degree the ability to respond to any change in the external factors that affect it. We call such changes stimuli. The greater the intensity of the stimulus the sharper is the response. When the intensity is extreme it may kill the cell. Stimuli are divided into ***chemical, mechanical, thermic, photic*** and ***electrical.***

The commonest manner in which a cell responds to stimuli is by way of **movement,** i.e., by a change in the form of the entire cell, or of some of its parts. The phenomena that may be observed are the ***amœboid movement, contraction,*** the ***movement*** of certain parts ***within the cell,*** and the ***movement of special accessory organs,*** such as cilia or flagella.

Amœboid movement can be studied best in the amœbæ, a family of the microscopic rhizopods, in the early stages of the development of the lower metazoa, and particularly in the lymphocytes of the blood of all the higher animals. At a certain place in the cell, which is globular when at rest, one or more processes protrude, and are either drawn in again or are followed by the body so that a change of location takes place. The movement is extremely slow (Pl. 1, Fig. 3, wz).

While the amœboid movement takes place in the protoplasm of the cell body, which is no further differentiated, **contraction** always occurs in certain differentiated formations of the cell body that usually run parallel through the cell, the contractile fibrils, and therefore differs from the former in always being in only one direction. These contractile fibers are met with in the higher animals only in quite definite tissue cells, those of the muscles, a description of which will come later.

Movements within the cell without change of its form are met with throughout the vegetable kingdom as protoplasmic currents, but in the higher animals they are to be seen only in the ***pigment cells.*** Pigment is usually found in cells in the shape of little, variously colored granules or rods, which either have been formed there as products of metabolism or are derivatives of the coloring matter of either the blood or the bile. They are distinguished by their content of iron and sulphur. Pigment occurs in all possible cells, but

plays its most important part in the cells of the connective tissue and of the epithelia. It determines the color of the skin, which is changeable in many animals. These changes of color are effected very often by photic causes, by exposure to or deprivation of sunlight. Guided by such stimuli the pigment either flows toward the periphery of the cells, spreads itself over the entire cell body, or flows back and agglomerates into a small, compact lump. We find something quite similar in the human retina.

The final form of movement is that which is exhibited by means of specially constructed accessory organs, more or less long and numerous threads that project from the free surface of the cell, known as **cilia** or **flagella.** While flagella serve as organs of locomotion to the protozoa and the young of many metazoa, moving the animal about in the water by their strokes, ciliated cells occur in the higher animals only in the linings of cavities, where their duty is to set in motion any fluid contained therein, and any foreign bodies that may happen to enter, by strokes made unceasingly in only one direction. The details concerning ciliated cells and the ciliary movement will be given in the description of the ciliated epithelium.

But the cell may respond to external stimuli not only through the production of mechanical energy; it may produce **light,** as is often seen in pelagic animals, or **heat,** or **electrical force,** but the latter is generally very slight and attains a considerable strength only in the so-called electric fishes, in which it is produced in special organs.

The Propagation of the Cell

The final, and perhaps the most important, property of the cell to be described here is its power to reproduce. Just as every cell is able to assimilate nutrient bodies brought to it from without and to utilize them in its growth, so is it able to produce new individuals of the same kind. Growth and reproduction are originally similar processes. If the supply of food and assimilation is in the long run greater than its need, the cell multiplies itself.

Cell increase is greatest in childhood; later, when the body has reached its full development, it gradually declines, but does not cease altogether until the death of the individual. All cells, with few exceptions, have a limited length of life, so they are constantly dying and being replaced.

The replacement is always secured through segmentation of the remaining cells, a process that involves both the cell body and the nucleus. While the division of the former takes place in the same way almost everywhere, that of the latter may be accomplished in one of two quite different ways: the **indirect division of the nucleus,** or **mitosis,** and the **direct division of the nucleus,** or **amitosis.** A feature common to both processes is that the nucleus is always the first to divide, and then, when its division is quite, or practically complete, the division of the cell body takes place. In indirect segmentation each of the daughter cells obtains an almost mathematically exact half of the mass of chromatin in the nucleus, but this is not the case in direct segmentation. Indirect segmentation plays by all means the greater part in the life of the cell, so we will describe it first.

Indirect Segmentation

As stated above, the most important constituent of the nucleus, its chromatin, is divided as exactly as possible into halves in indirect segmentation. First, the chromatin that is scattered about in the nucleus in larger or smaller particles collects together to form a long thread, which breaks into a certain number of pieces of equal length, and then each piece splits longitudinally into equal parts. Each daughter nucleus receives one-half of each of these pieces. In addition the central bodies separate, so that each daughter cell contains one of them.

Fig. 2.—Indirect Segmentation of the Nucleus (stage of the spirem).

The process of indirect segmentation is commonly divided into three successive stages: the ***prophase,*** the ***metaphase,*** and the ***anaphase.***

In the **prophase** the chromatin scattered about in the nucleus collects together, ranging its granules close together so as to form a dense chromatic network (Pl. 4, Figs. 11 and 12). The threads of this network give way in numerous places and the substance composing them collects in other places, until finally a single long thread of chromatin is produced, which runs through the nucleus in numberless convolutions (Pl. 4, Fig. 13). Its surface is at first irregular and rough, but gradually becomes smooth, and the nucleus enters the stage of the spirem, or ball of smooth thread, which very soon breaks down into a number of pieces of equal length, the **chromosomes.**

The number of chromosomes is constant for each genus of animals, and varies from two and four in the intestinal worm of the horse (Pl. 4, Fig. 15), to over a hundred in many anthropods. The human cell, like that of many other mammals, contains twenty-four chromosomes. They stain with basic dyes more intensely—that is, they are more basophilic—than the chromatin of the resting nucleus; this is to be ascribed to a higher content of free nucleinic acid.

Fig. 3.—Indirect Segmentation of the Nucleus (stage of the formation of the pole field).

Very soon after the formation of the chromosomes changes take place in their shapes and in their positions in the nucleus. They bend into more regular loops, with the convexity of each loop facing in one direction, the two free ends in the opposite.

During this stage, or earlier in many cases, the nuclear membrane gives way and permits the chromosomes to lie free in the cell body. The nucleolus disappears; what becomes of it no one yet knows with certainty.

The central bodies play an extremely important part and undergo a considerable change in the prophase. At this time they lie in the so-called **polar field,** i.e., at the place in the cell toward which the convexities of the chromo-

somes are directed. Even in cells that show no traces of archoplasm when at rest, a **system of rays** develops about each, radiating in all directions. Part of these archoplasmic rays are lost in the indifferent cell protoplasm, part attach themselves to the chromosomes that now lie free in the cell. This picture soon changes as the central bodies, which have been lying close together, now separate, one moving toward one pole of the nucleus, the other toward the opposite. Each takes with it its archoplasmic radiation, which causes each to resemble a sun gliding along what was formerly the nuclear membrane. They are also connected by archoplasmic rays which stretch out between them. Therefore, when the central bodies have arrived at the poles of the nucleus, we can distinguish three kinds of archoplasmic fibers: first, those that radiate from the central bodies and are lost in the cell protoplasm, the ***polar spindle fibers;*** second, those that join the central bodies to the chromosomes, the ***traction,*** or ***mantle fibers;*** third, those that pass from one central body to the other, the ***central spindle fibers.***

As soon as the central bodies have reached the poles of the nucleus the chromosomes change their places until they are arranged in one plane with the convexities of all the loops directed inward, the free ends outward. Seen from the side this extraordinarily characteristic stage of mitosis gives the picture of a plate occupying the equator of the cell, the **equatorial plate** (Pl. 4, Fig. 14), while when seen from above it often presents a remarkably regular star, the **mother star,** or **monaster** (Pl. 4, Fig. 15). The central spindle fibers extend from one central body to the other directly through the equatorial plate; the mantle fibers pass, like the rods of two open umbrellas tilted toward each other, from each central body to the ends of the chromosomes. This ends the prophase and the mitosis enters the **metaphase.**

Although the exact division of the entire quantity of chromatin is essentially facilitated in the prophase by the formation of chromosomes, i.e., by the collection of the particles of this substance scattered about in the nucleus and its separation into a certain number of equal portions, yet the division is made complete in the metaphase by the splitting of each chromosome longitudinally into two halves, each mother chromosome thus becoming two daughter chromosomes of equal size. This does not always take place in exactly the same stage of mitosis; it may be consummated during the prophase before the chromosomes form the monaster, and then the daughter chromosomes lie parallel to each other for a much longer time, but usually the splitting occurs in the beginning of the metaphase, when the stage during which the daughter chromosomes lie near together is short and cannot always be easily observed (Pl. 5, Fig. 16).

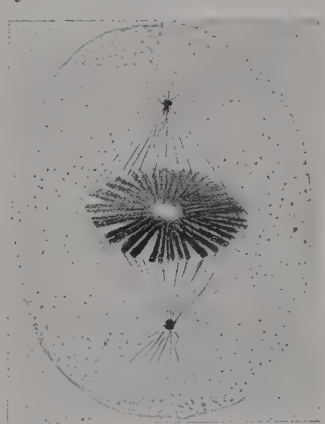


Fig. 4.—Indirect Segmentation of the Nucleus (stage of the monaster).

Now the daughter chromosomes separate, one moving with its convexity in front toward each central body (Pl. 5, Fig. 17). It is not quite correct to say that the chromosomes move, for they can scarcely have an active motil-

ity; it is more probable that the central bodies form fixed points from which contractile spindle fibers, particularly the mantle fibers, extend to and are inserted into the ends of the chromosomes, and that the movements of the latter are due to the contraction of these spindle fibers. Some investigators doubt this, and believe that the central bodies are kinetic centers which exert an influence over the chromosomes comparable with that exerted by a magnet over bits of iron, in which case the spindle fibers may be the visible phenomenon produced by this force, like the lines of magnetic power shown with iron filings.

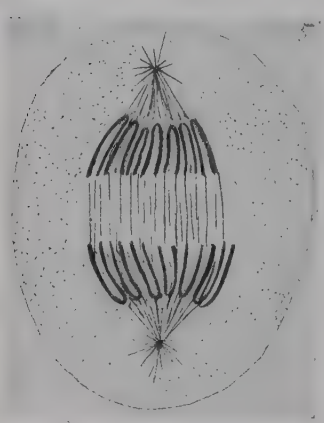


Fig. 5.—Indirect Segmentation of the Nucleus (barrel stage).

As stated above, the daughter chromosomes move with their convexities forward. This brings the convexities of all toward the central bodies, their free ends toward the equator of the cell, and results in a figure not unlike a barrel. We speak of this as the ***barrel stage*** of the mitosis. Apparently it lasts quite a while, for it may be observed very easily and often. The three portions of the spindle fibers can be differentiated very distinctly. The polar fibers extend from the central bodies to the periphery of the cell, the mantle fibers, which are very short, to the chromosomes, while the central spindle fibers run approximately parallel between the free ends of the daughter chromosomes. They naturally cross the equator of the cell, where each has a little nodule. These nodules, taken together, form a plate situated in the equator, the **cell plate.** The barrel stage now passes over into that of the **daughter stars,** in which the daughter chromosomes are arranged in stellate figures.

In the **anaphase** the division of the cell body is completed and the two daughter stars are changed into two resting nuclei. The ***division of the cell body*** takes place at the equator of the cell. A circular furrow appears and cuts deeper and deeper into the cell body. Shortly before the division is complete a little heap of granules is formed by the compression of the bundle of spindle fibers and the consequent crushing of the cell plate, from which the central spindle fibers radiate in each daughter cell to the chromosomes.

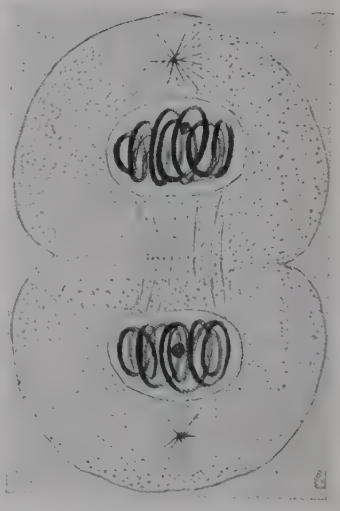


Fig. 6.—Indirect Segmentation of the Nucleus (stage of the daughter spirem).

The transformation of the daughter stars into **two resting nuclei** is quite similar to a reversal of the prophase. The chromosomes turn their convexities toward the central bodies again and unite to form a thread that is at first smooth, later irregular (Pl. 5, Fig. 18). Threads of chromatin grow out from the irregularities of the thread and join to form a network.

The chromatin also forms a chromatic membrane at the periphery of the nucleus, inside of which it breaks into little particles which fit into the linin framework that now appears (Pl. 5, Fig. 19). The nucleolus reappears together with the chromatic membrane, while the central bodies and the spindles likewise pass through retrograde changes. The mantle fibers disappear completely, as does the central spindle, the granular plate of which is demonstrable for a while as a little corpuscle between the two daughter cells. Finally the central bodies part and each seeks its characteristic situation in its own cell. Then we have two resting daughter cells, each of which is in every way like the mother cell, through the segmentation of which they originated.

Indirect segmentation is to be met with wherever tissue growth is taking place or dead cells have to be replaced, and is a sign that the cells are vigorous. This is not always true of direct segmentation, which is often to be seen where living cells have been destroyed.

Direct Segmentation

An accurate halving of the chromatin is not contemplated in direct segmentation, which takes place either with the formation of a ***constriction,*** or by a process of ***budding,*** with subsequent fragmentation of the nucleus. In the former case the nucleolus divides, the two daughter nucleoli separate, while at the same time the nuclear membrane presents a more or less regular, circular, constricting furrow. The two halves of the nucleus separate, the connecting pedicle becomes longer and thinner until it breaks, leaving two separate nuclei, each accompanied by a nucleolus. In budding a little lump appears on the surface of the nucleus, enlarges more and more, and cuts itself off from the mother nucleus after it has enclosed a nucleolus. Budding very often occurs at several places on the surface of the nucleus, so that the latter is finally broken up into a large number of daughter nuclei, it is *broken into fragments.* The buds may remain for a long time connected with the mother nucleus by threadlike bridges, so the pictures produced may be remarkably multiform.

In many cases the central bodies also appear to take an active part in the amitosis, in that they interpose themselves between the two halves of the nucleus and accelerate the process (Pl. 2, Fig. 5).

In mitosis the division of the cell body almost always follows or accompanies that of the nucleus, but in amitosis no such division of the cell body takes place, as a rule, so this process leads to the formation of ***polynucleated cells.***

Amitotic segmentation is to be observed chiefly in the colorless blood cells, but it may also be seen in the epithelium of the bladder, and in the cells of the liver.

Finally, it should be mentioned that *transition forms between mitotic and amitotic segmentation* have been described in which the constriction through the nucleus takes place after the chromatin within it has collected into a regular form, but without the development of chromosomes.

B

THE TISSUES

Now that we have studied cells, which are the elementary constituents of the animal body, we will proceed to the next higher unit, the tissues that are formed from them. **We understand by a tissue a complex of cells which present the same individual characteristics.** During the first stages of development all of the cells of the embryonal body are remarkably alike, though perhaps not perfectly the same, but very soon they separate into groups that have common individual characteristics. They assume definite arrangements, and form special characteristic structures within their cell bodies, or develop special intermediate substances between themselves. The tissues thus started naturally have to perform the various duties of the entire organism, so to each is assigned distinctly defined functions.

Tissues are commonly divided into four distinct groups:

1. Epithelial;
2. Muscular;
3. Nervous;
4. Connective.

The cells themselves play the essential parts in the epithelial, muscular, and nervous tissues, in which only an insignificant intercellular substance is developed, but the condition is quite the reverse in connective tissue, in which the development of the cells is subordinated to that of the intercellular substance.

With regard to the derivation of the various tissues from the three primitive organs of the embryo, all three—ectoblast, mesoblast, and entoblast—give rise to epithelial tissue. Muscular tissue comes mainly from the mesoblast, and only to a slight degree from the ectoblast. Nervous tissue comes exclusively from the ectoblast. Connective tissue arises from the mesoblast, the entoblast, and probably also from the ectoblast.

EPITHELIAL TISSUE

Epithelial tissue consists almost wholly of cells placed together in rows, which differ both in their mode of arrangement and in their special construction. As its name indicates, it covers the other tissues, separating them from the outer world and lining all the cavities of the body. Thus it forms an extremely important ***protection.*** In addition to this function it has another which is perhaps equally essential, to provide for the ***secretions*** and ***excretions*** of the body, so the processes of metabolism that have been described play a particularly great part in their cells. To attain this end the epithelium of the surface of the body, and more especially that lining its cavities, is invaginated to form **glands.** A third function of the epithelial tissue is to receive stimuli that fall upon the body.

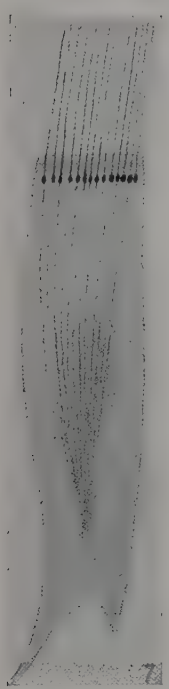


Fig. 7.
Ciliated Cell.

Each epithelium has a **free surface,** which looks outward, or, in a cavity, inward, and a **base** with which it rests upon the subjacent tissue. It is usually separated from the latter by a thin, structureless membrane called the **basal membrane.** Special formations that serve various purposes may develop on the surfaces of the epithelial cells, chief among which are the **cilia.**

Cilia are fine filaments that project from the free surfaces of these cells and maintain during life a constant movement in a fixed direction. Although they are always rather short in man, they attain quite a length in the lower vertebrates and in the invertebrates, where they are often considerably longer than the cell itself (Pl. 9, Figs. 28 and 29). In the lower animals a single cilium may project from a cell, or several may coalesce to form a sort of whiplash, as in a **flagellated cell** (Pl. 10, Fig. 30), but in man we always find many cilia of equal length standing close together. The free surface of the ciliated cell is provided with a homogeneous band of protoplasm through which each cilium passes to the outermost periphery of the cell, where it terminates in a little nodule, the so-called **basal corpuscle.** In many cases the cilia continue in the cell body as fine, converging threads to the base of the cell, thus forming the **root of the cilia.**

Ciliated epithelium is found throughout the entire respiratory tract, as far as the smallest bronchi, the tympanic cavity, the auditory canal, the central canal of the spinal cord, the uterus, and the efferent ducts of the epididymis.

The construction of the so-called **hair cells,** found in the cristæ and maculæ acusticæ of the membranous labyrinth, is very similar to that of the ciliated cells in principle, but basal corpuscles are absent and, as the hairs have no movement of their own during life, we must consider these corpuscles to be the kinetic centers of ciliary movement.

The so-called **cuticular band** appears as a thin layer on the free surface

of epithelium beyond the crusta. It may seem to be homogeneous and without structure, as in the ciliated cells, or it may have a fine, transverse striation, caused by the presence of many short rods, processes of the cell protoplasm, when it is called a **rod band.** Such a rod band is met with in the epithelial cells of the intestine (Pl. 9, Fig. 27; Pl. 8, Fig. 26), and is probably connected with the absorption of certain nutritious substances by the intestinal epithelium. This is indicated by the fact that it is met with in different conditions of development during different phases of absorption. Similar formations occur on the epithelial cells of certain sections of the uriniferous tubules, where the rods are coarser and can be seen more distinctly than in the intestinal epithelium. Such a formation is called a **bristle band** (Pl. 6, Fig. 21). The relations of these rods to the activity of the cell are more evident here, for the bristle band is present only on the secreting cells and is absent on the inactive ones. Still longer processes are met with on the epithelial cells of certain sections of the epididymis, where they closely resemble cilia, except for the absence of basal corpuscles.

The bodies of the epithelial cells also undergo considerable modifications in form and structure to accord with the particular duties they have to perform. Wherever the main duty of the epithelium is to act as a *protective covering,* as over the outer surface of the body, the superficial portion of the cell body is transformed into **keratin,** and the cell becomes horny. The hair and nails consist essentially of such cornified cells. A ***calcareus epithelium,*** the **enamel,** covers the crowns of the teeth and gives them their great hardness and power of resistance.

Another function of epithelial tissue, aside from the glandular epithelium which will be described later, is that of ***absorption*** and ***secretion.*** It is mainly through the latter power that epithelial cells bring about very striking and important changes in the body. The chief secretory product of these cells is **mucus,** which, in the epithelium of the intestinal canal and of the respiratory tract, is elaborated from the protoplasm within the cell by the **mucinogen granules.** These can be distinguished from the granules of the cell protoplasm by their higher refractive power, and particularly by the fact that they are not oxyphilic, but are basophilic, and therefore stain with basic instead of acid dyes. During the further course of the formation of mucus these mucinogen granules increase in size and number, while the protoplasm between them changes its staining reaction and becomes basophilic. The granules develop chiefly in the distal portion of the cell, near the free surface. This portion becomes considerably distended by the great accumulation of mucinogen granules, bulges, and contrasts sharply with the proximal, more slender part of the cell, which, as a whole, now has the shape of a goblet. Such cells, filled with mucus, are called **goblet cells** (Pl. 8, Fig. 26; Pl. 9, Fig. 29). The slender proximal portion contains unaltered protoplasm and the nucleus, which is usually more or less deformed by pressure. The surface of the cell ruptures when the process within it reaches its acme, probably because the contents are caused to swell by the admission of water, and the mucus, i.e., the mucinogen granules plus the intergranular substance, pours forth as a homogeneous or a filamentous mass into the interior of the cavity lined by the epithelium. The

empty and collapsed cell refills with oxyphilic protoplasm from its proximal portion, after which it differs in no way from the adjacent epithelial cells, in one after another of which the same process takes place.

The secretory activity of the epithelium may also result in the destruction of the cells that take part; they are compressed by their vigorous neighbors and cast off. The process of casting off is still more marked in the true protective epithelia, such as that of the cornea, or of the mouth. The cells thus cast off must be replaced of course, and this replacement is accomplished by indirect segmentation of the remaining cells (Pl. 10, Fig. 31).

Epithelial cells are divided according to their shapes into **flat, cuboidal, cylindrical,** and **polymorphous.** A flat cell is one in which the breadth greatly exceeds the height; a cuboidal, one in which the breadth and height are approximately equal; a cylindrical, one in which the height greatly exceeds the breadth. A flat cell therefore has about the shape of a tile, such as are frequently used for floors; a cuboidal cell that of a dice, or often that of a prism in which the transverse is about equal to the vertical diameter; the cylindrical cell that of a prism which has been much lengthened along its longitudinal axis. The bodies of the polymorphous cells are irregularly polyhedral, and are often provided with numerous short offshoots. Sometimes they look like open umbrellas, whence they are called umbrella cells.

As regards the way in which epithelial cells are connected, it has already been said that they lie close together in the epithelium. Their smooth surfaces may be pressed together so very closely as to leave no visible apertures, and special methods of preparation are necessary to enable us to demonstrate an intermediate substance, the **cement,** or **intercellular substance.** This is present particularly wherever flat cells unite in a single layer to form an epithelium, and is very easily stained black with silver salts. Such a silvered epithelium shows on its surface a network of fine lines which mark the intercellular substance. The meshes of the network are the bodies of the epithelial cells (Pl. 6, Fig. 20).

In other cases the interspaces between the individual cells are rather large and form **intercellular spaces** and **clefts,** which are filled during life with tissue fluid. These clefts are closed at the free surface by edges of firm intercellular substance interposed between the tops of the cells. These so-called **cement edges** can also be easily stained, and then the surface may present a picture very like that given by the intercellular substance of flat epithelium (Pl. 8, Fig. 25).

Another interesting condition is to be found frequently. Such intercellular clefts may contain narrow bridges of protoplasm that unite the cell bodies. These are called **cell bridges,** or **intercellular bridges.** When these are present we can no longer speak logically of individual cells, for the entire epithelium forms a single large mass of protoplasm, a **synctium,** in which the nuclei lie scattered about. Such cell bridges are to be found in many epithelia, but not in all, as has frequently been claimed. The intercellular clefts are of importance to the epithelium in that they enable nutrient fluid to enter between the cells (Pl. 11, Fig. 32).

Cell bridges are formed of ordinary cell protoplasm, but fibrous differentia-

tions of the cell body, the so-called epithelial fibers, may pass through them. These fibers develop chiefly in the superficial layers of the cell protoplasm and, in their courses, pass through not only one, but quite a number of cell bodies. They have a considerable importance in dense epithelia in that they increase the power to resist external forces.

We come now to the mutual position of the cells from which the common classification of the different kinds of epithelium as ***simple, stratified,*** and ***stratiform,*** is derived.

Simple Epithelium

Simple epithelia, i.e., those formed of single layers of cells, may be flat, cuboidal, or cylindrical, in accordance with the type of the cells of which they are composed.

Simple flat epithelium consists of thin, tilelike cell bodies, the lateral surfaces of which are in apposition one with another. The cell plates are often so thin that the nuclei produce elevations on the free surface. The cells do not have straight lateral margins, as a rule, but irregular ones that fit one into another, while between them lies an intercellular substance which forms a network of irregular, fine trabeculæ (Pl. 6, Fig. 20). Cilia are never found on simple flat epithelium, but epithelial fibers may be seen in the cell bodies running parallel to the free surface only. Flat epithelium is distributed very widely throughout the human body; it lines all of the serous cavities, like the pleura, the pericardium and the peritoneum, and also the entire vascular system, the heart, arteries, veins, capillaries, and lymphatics. In both of these places it is frequently known as **endothelium.** Other flat epithelia are the respiratory epithelium of the alveoli of the lungs, the indifferent parts of the epithelium of the labyrinth, and the endothelium of the cornea. In the last may be found cell bridges and epithelial fibers.

Fig. 8.—Simple Flat Epithelium (schematic).

Simple cuboidal epithelium is glandular epithelium *κατ ἐξοχήν*. The expression cuboidal must not be taken too literally, for, aside from the fact that the cells are almost always bounded by more than four sides and therefore resemble prisms rather than dice, they may often assume the form of truncated cones or pyramids with their bases resting on the basal membrane. As we shall see later, this is the case particularly in the glands, where many cells are grouped into a relatively small space (Pl. 3, Fig. 8). Cuticular formations, cilia, and bristles are to be found on simple cuboidal epithelium (Pl. 6, Fig. 21). ***Intercellular clefts*** and ***cement edges*** are quite generally present. The nucleus lies either near the center of the cell, or toward its proximal end. Such cuboidal epithelium is found in most glands, as has been already mentioned, where it is secretory. It has a respiratory function in the bronchioles, and is provided with cilia in the minute bronchi

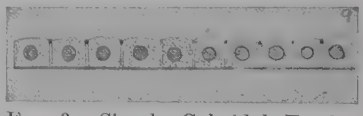


Fig. 9.—Simple Cuboidal Epithelium with Intercellular Spaces and Cement Wedges (schematic).

and in the tympanic cavity. The epithelium of the choroid plexus of the brain is also simple cuboidal and has cilia during embryonal life.

Simple cylindrical epithelium consists of a single layer of elongated cells which have a more or less regular prismatic form. As a rule, the cells are not of the same transverse diameter throughout their length, but become more slender toward their proximal ends, which lie upon their basal membrane (Pl. 8, Fig. 26; Pl. 9, Fig. 27). Intercellular spaces closed in with cement almost always exist between the cells. Cell bridges also may be observed. In the lower epithelium the nucleus usually lies near the base of the cell, in the higher nearer the center. Goblet cells are often interposed between the true cylindrical ones (Pl. 8, Fig. 26). The free surface often has a cuticular band, more rarely cilia (Pl. 9, Fig. 28). This is the characteristic epithelium of the gastrointestinal canal, which it lines from the cardiac orifice of the stomach to the anus. In the stomach all of the cells are filled with mucus, in the intestine the ordinary cylindrical cells have many goblet cells between them. The former have on the free surface a cuticular band composed of short rods, and are preeminently absorptive. Simple cylindrical epithelium also lines the excretory ducts of the large intestinal glands, the liver and the pancreas, the bile duct, the cystic duct, the gall bladder, the hepatic duct, and the pancreatic duct. At the entrances of these excretory ducts into the glands the cylindrical cells become shorter and at last cuboidal, or, in the case of the pancreas, flat. Finally we meet with a simple cylindrical epithelium in the excretory passages of the sexual glands; in males in the vas deferens, the seminal vesicles, the ejaculatory duct, and in many parts of the urethra, in females in the Fallopian tubes, and in the uterus, where part of the cells have cilia.

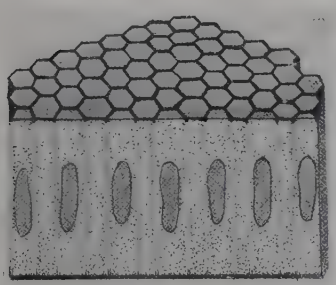


Fig. 10.—Simple Cylindrical Epithelium with Intercellular Spaces and Cement Wedges (schematic).

Stratified Epithelium

A stratified epithelium consists of two or more layers of cells, none of which extend through its entire thickness, i.e., none of them has one end at the free surface and the other at the basal membrane. The number of cells placed one over another is very variable; in the simplest cases it is two, but in very thick epithelia it may be twenty or more. True stratified epithelia are never ciliated. They are classified according to the cells of which they are composed into stratified flat epithelium, transitional epithelium, and stratified cylindrical epithelium.

Stratified flat epithelium always shows an unmistakable regularity in its construction. The deepest, proximal layer consists of cylindrical cells of greater or less height, on which rest distally one or more layers of polymorphous cells, and the epithelium is completed at its free surface by one or more layers of quite flat cells (Pl. 10, Fig. 31). Between the cells are very distinct ***intercellular spaces,*** through which pass **cell bridges** (Pl. 11, Fig. 32). As the

isolated cells, when torn apart, seem to be provided with numerous short processes they have been termed **prickle cells,** or **crenated cells. Epithelial fibers** are particularly prominent in stratified flat epithelia, in which they run vertically through its entire thickness from base to surface, and then bend over to form arches. The flat cells in the most superficial layer are usually *horny.* Stratified flat epithelium is always a protective covering without secretory functions, and as such it covers the entire surface of the body under the name of **epidermis.** Stratified flat epithelium also covers the anterior surface of the

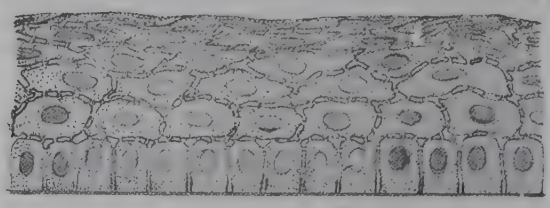


Fig. 11.—Stratified Flat Epithelium with Intercellular Spaces and Intercellular Bridges (schematic).

cornea, is present at the entrances and exits of the digestive, respiratory, and genitourinary organs, and lines the mouth, fauces, vestibule of the nose, the navicular fossa of the penis, the female urethra, the vagina, and the portio vaginalis of the uterus. We also find it in the external auditory canal, on the vocal cords, and on the posterior surface of the epiglottis.

Transitional epithelium is very like the preceding, but the strict regularity in its construction is wanting. The proximal layer of cells is not so typically cylindrical, and the most distal layers are not so markedly flat. Its

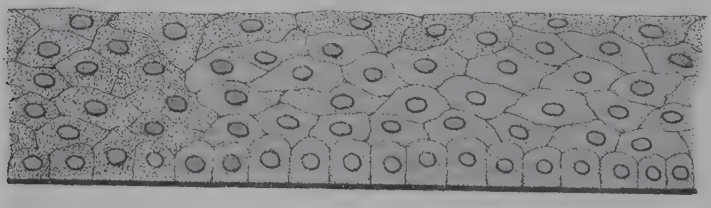


Fig. 12.—Transitional Epithelium (schematic).

free surface is usually covered by a layer of polymorphous cells, which we call ***cover cells,*** or ***umbrella cells,*** from their form (Pl. 11, Fig. 33). Cornification, intercellular spaces, and epithelial fibers never occur in this form of epithelium, which is found only in the urinary passages, the pelvis of the kidney, the bladder, and the prostatic portion of the male urethra.

Stratified cylindrical epithelium is of still rarer occurrence. It is always composed of only a few layers of cells, the most proximal of which are small and cuboidal, with a row of conical cells resting their bases upon them.

The apices of these conical cells point toward, but do not reach the free surface, while between them lie the true cylindrical cells with their proximal ends pointed, and their distal ends bounding the free surface. The middle layer may be wanting, and then the cylindrical cells lie directly on the cuboidal. Stratified

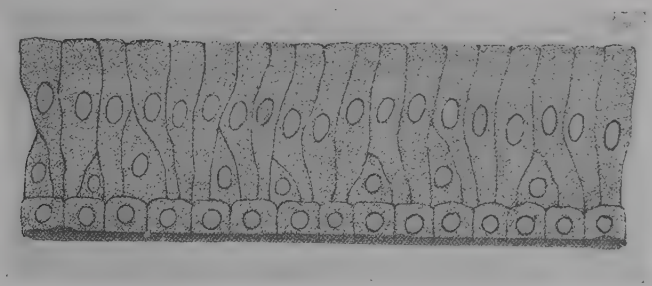


Fig. 13.—Stratified Cylindrical Epithelium (schematic).

cylindrical epithelium is never ciliated in man, in whom it is found lining the submaxillary and parotid ducts, the membranous and cavernous portions of the male urethra, and the palpebral conjunctiva.

Stratiform Epithelium

We call an epithelium stratiform when all of the cells in it either start from the basal membrane and only a part of them reach the free surface, or start from the free surface and only a part reach the basal membrane, while the rest end within the epithelium. An epithelium like this cannot be said to be stratified, although it may easily be mistaken to be such, particularly when the nuclei lie in rows one above another. In stratiform epithelium we have to do with only two varieties of cells, one of which is long, cylindrical, and reaches

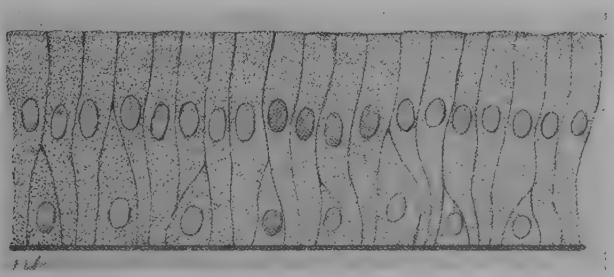


Fig. 14.—Stratiform Epithelium (schematic).

from the surface to the basal membrane, while the other is crowded in between these at either the superficial or deep surface.

Such a stratiform epithelium is the **ciliated,** found in the respiratory organs from the vestibule of the nose to the smaller bronchi, where it gives place to a simple cuboidal epithelium (Pl. 9, Fig. 29; Pl. 11, Fig. 35). The ciliated cells pass through its entire thickness and taper very much proximally, while between their tapering ends lie conical cells with their broad bases on the basal

membrane and their apices lost between the ciliated cells. Goblet cells in the same situation as the ciliated cells are often met with in this epithelium. Stratiform ciliated epithelium is also found in the Eustachian tube, in the epididymis, and in the spermatic ducts.

The **sensory epithelium** of the membranous labyrinth is stratiform, but the conditions present are the reverse of those in stratiform ciliated epithelium. Long, slender cells, with their nuclei in their proximal thirds, pass through the entire thickness of the epithelium, and rest with broad bases on the basal membrane. Between these slender, so-called **filiform cells,** which serve as supports, lie broader, prismatic cells that reach from the free surface only to about the middle of the epithelium, and carry on their distal ends shorter or longer hairs, the auditory hairs. The nucleus of each of these **hair cells** lies in its proximal portion. Thus the nuclei of the epithelial cells form several rows, those of the auditory cells the most distal one, those of the filiform one or more proximal.

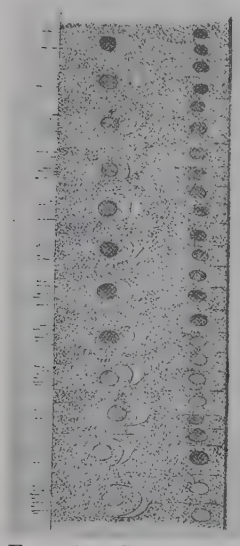


Fig. 15.—Sensory Epithelium of the Membranous Labyrinth of the Ear (schematic).

It should be mentioned in conclusion that there are a few kinds of epithelium that do not conform to this classification. Among these in man is the **spermatozoa producing epithelium** of the seminiferous tubules, which is composed of several superimposed layers of roundish cells, the seminal cells, with the long Sertoli's cells between them extending from the basal membrane to the lumen of the canal.

The **retina** is a sensory epithelium that, very like the auditory, contains supporting cells, known as Mueller's fibers, which pass through its entire thickness, but instead of forming a single layer, as in the ear, the sensory cells are in several layers, one over another, and are provided with many long offshoots.

Glandular Epithelium and Glands

Although epithelial cells in many places have a secretory function, yet most of the secretion and excretion in the human body is performed by special epithelial formations known as glands, and not by the superficial epithelium. We mean by a gland ***a proliferation of the epithelial tissue that takes place, as a rule, below the level of the epithelium, the essential object of which is to obtain an enlargement of the secreting surface.***

In the great majority of cases these proliferations are hollow, and are therefore invaginations of the superficial epithelium. A **glandular cavity,** that varies a good deal in shape, is formed and is lined with **glandular cells,** which empty their secretory products into it. The primary opening of this cavity usually remains patent, so that the secretion is poured through it over the surface of the epithelium. The system of cavities in a gland may be very extensive, and different portions may assume different functions; in such cases

the parts distant from the surface are devoted mainly to secretion, while those in immediate proximity to it serve simply to carry the secretion away, and the gland becomes thus divided into a *secretory* and an *excretory portion.*

But the open connection between the glandular cavity and the surface of the epithelium does not remain patent in all cases. It may become obliterated, and then we have a **closed gland** beneath the surface, the secretion of which is carried away by the lymph and blood channels.

These true glands with glandular cavities contrast with others in which epithelial cords proliferate deeply, have no cavities from the first, and do not become canalized later. Such are known as **solid glands.** The vascular system must care for their secretions, as well as for those of the closed glands, so both varieties are included under the name **hæmatopoietic glands.**

We will now familiarize ourselves more closely with the details of the true, open glands.

The True Glands

Every true gland originates in a depression of the superficial epithelium in one of two principal ways. In one form the invagination, with its peculiar glandular epithelium, is of approximately the same transverse diameter everywhere, so that in its simplest type it resembles the finger of a glove; in the other it forms a little hollow ball. The former we call a ***tubular,*** the latter an ***alveolar gland.*** These two simple, fundamental types are complicated in many ways. The gland may ramify, or many glands may unite to form a single large one, and therefore we have ***simple, branched,*** and ***compound glands.*** The free ends of tubular glands may also dilate and give rise to a mixed variety known as ***alveotubular glands.*** We will now study each of these varieties.

The **simple tubular gland** is a short, straight, or slightly curved, blind tube that passes from the surface of the epithelium down into the subjacent tissue. At its mouth the superficial epithelium changes gradually into glandular. Lieberkuehn's intestinal crypts are examples of such very simply constructed glands (Pl. 53, Fig. 126).

Fig. 16.—Simple Tubular Gland (schematic).

Convoluted glands are distinguished from the foregoing by the considerably greater length of the glandular tube, and the fact that the latter has numerous windings at its blind end, which form a convolution of a glomerule. In consequence of its great length the tube is divided into a convoluted, secretory portion, and a straight excretory duct. Such are the sweat glands of the skin (Pl. 93, Figs. 197 and 198).

In the **simple branched tubular gland** the tubular invagination soon divides into two or more branches that lie close together, penetrate deeply and have blind ends. The simple initial portion usually remains lined with the superficial epithelium, and narrows just in front of the place of division, forming what is known as the **neck of the gland.** The branched parts, or **body of the**

gland, follow straight, or slightly tortuous courses, widen a little at their blind ends to form the **base of the gland,** and are lined with secretory epithe-

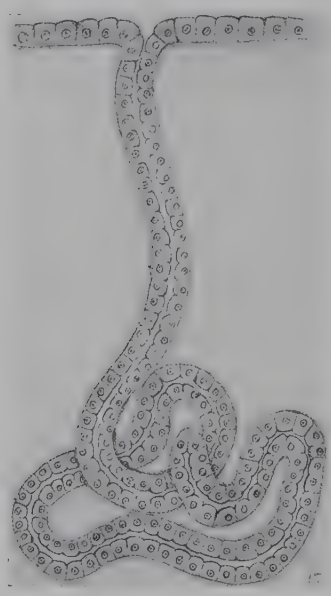


FIG. 17.—Sweat Gland (schematic).

FIG. 18.—Simple Branched Tubular Gland (schematic).

lium. The fundus glands of the stomach and the glands of the uterus are of this type (Pl. 50, Fig. 119).

Compound branched tubular glands are formed by the union of many glands of the kind just described, which empty their secretions into one

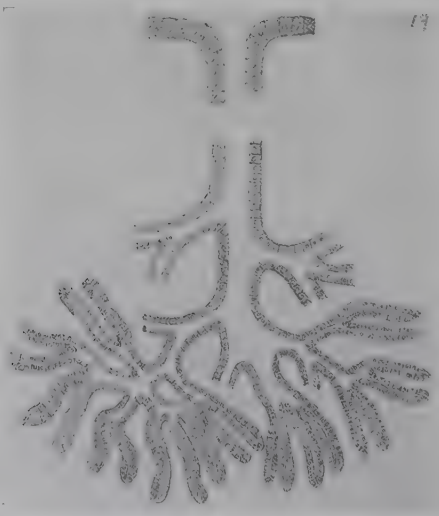


FIG. 19.—Compound Branched Tubular Gland (schematic).

or more common outlets. In such glands as these the glandular tubes may reach extraordinary lengths, while their different sections may assume various

secretory, and, under certain circumstances, absorptive functions. Such are the serous glands of the tongue, the lacrimal glands, the kidneys and the testicles (Pl. 58, Fig. 138; Pl. 61, Fig. 146). The liver also is one, but it

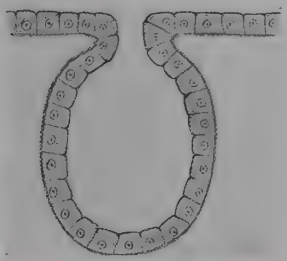


Fig. 20.—Simple Alveolar Gland (schematic).

Fig. 21.—Simple Branched Alveolar Gland (schematic).

differs from the others in that the branching canals unite to form a network within it.

The **simple alveolar gland** is a little vesicle lined with secretory cells

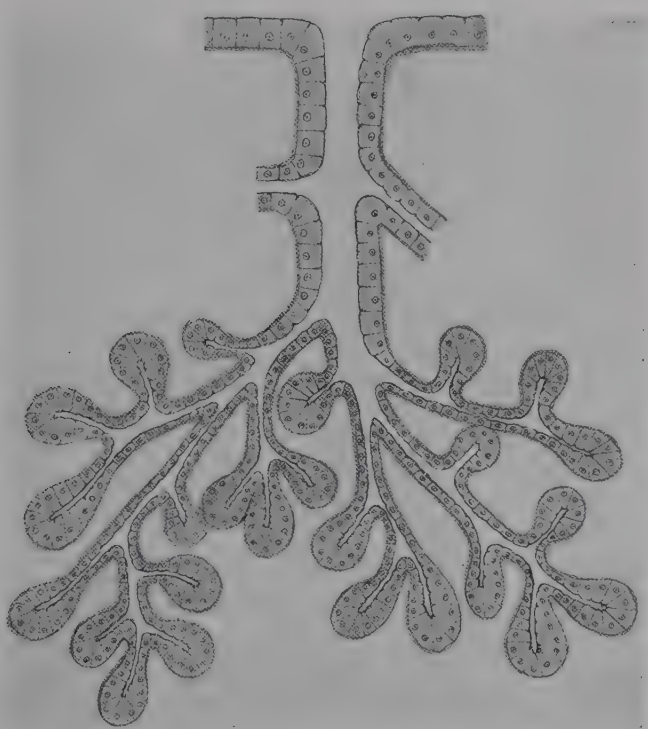


Fig. 22.—Compound Branched Alveolar Gland (schematic).

beneath the epithelium. It may be spherical or oval in shape. It communicates with the free surface by a narrow neck, where the secretory epithelium

becomes very thin and changes into the superficial. The only simple alveolar glands are the little sebaceous glands of the skin.

Fig. 23.
Simple Alveotubular Gland (schematic).

When two or more such simple alveoli empty into a common duct we have a **simple branched alveolar gland.** The efferent duct may be short with all the alveoli grouped at its end, or it may be long, with the alveoli attached along its sides. The large sebaceous glands of the skin are of the first type (Pl. 94, Fig. 201), the Meibomian glands of the lids of the second (Pl. 90, Fig. 193).

Many branched alveolar glands may unite, in the same way as the tubular, and then we have a **compound branched alveolar gland.** The excretory part of these glands, which are all large, is greatly developed and is divided sharply from the secretory part, which is confined to the alveoli. The alveoli empty into the primary efferent ducts, several of which join to form a secondary duct, and so on until finally we come to the principal excretory duct. The alveoli may communicate with the primary duct by short wide openings, or by long, narrow channels, when they seem to hang by slender pedicles and resemble grapes to such an extent that these are also called **acinous glands.** The mamma is an example of the former variety of compound branched alveolar gland (Pl. 98, Fig. 208), while the pancreas is a typical acinous gland (Pl. 55, Fig. 132).

Therefore, the most important part, the secretory portion, of a tubular gland has the form of a tube, that of an alveolar gland the form of a globule. The alveotubular is a mixed variety, the origin of which is thought to be an alveolar dilatation of the blind end of the secretory tubule.

The **simple alveotubular gland** needs no further description of its structure. The secretory epithelium adjoins the superficial and extends throughout the tubule and the alveolus. The tube is usually constricted like a neck at the junction of the superficial and the glandular epithelium. The pylorus glands of the stomach are of the type of the simple, and frequently of the branched alveotubular gland (Pl. 50, Fig. 121).

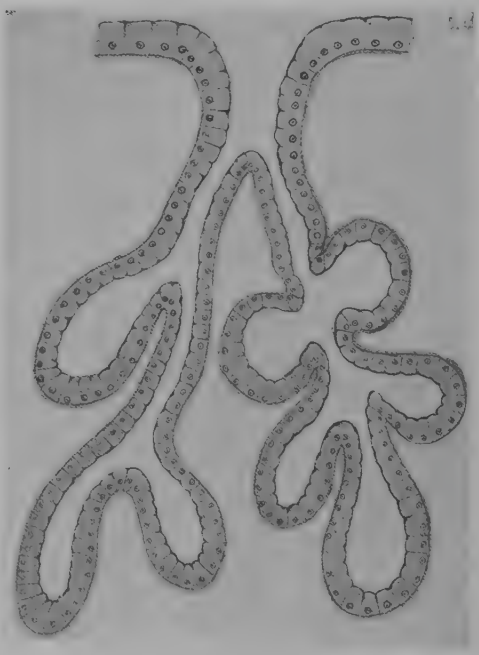


Fig. 24.—Branched Alveotubular gland (schematic).

A short excretory duct is formed in the **branched alveotubular gland.**

The secretory tubules branch not only end in alveoli, but are also studded with them. Littré's glands of the male urethra exemplify this variety.

Many of the glands already mentioned unite to form a **compound branched alveotubular gland.** Here we usually find a long excretory duct, lined with indifferent epithelium, which presents many branches. The indifferent is replaced by secretory epithelium in branches of a certain caliber. At the end of each tubule are groups of spherical or oval alveoli, usually

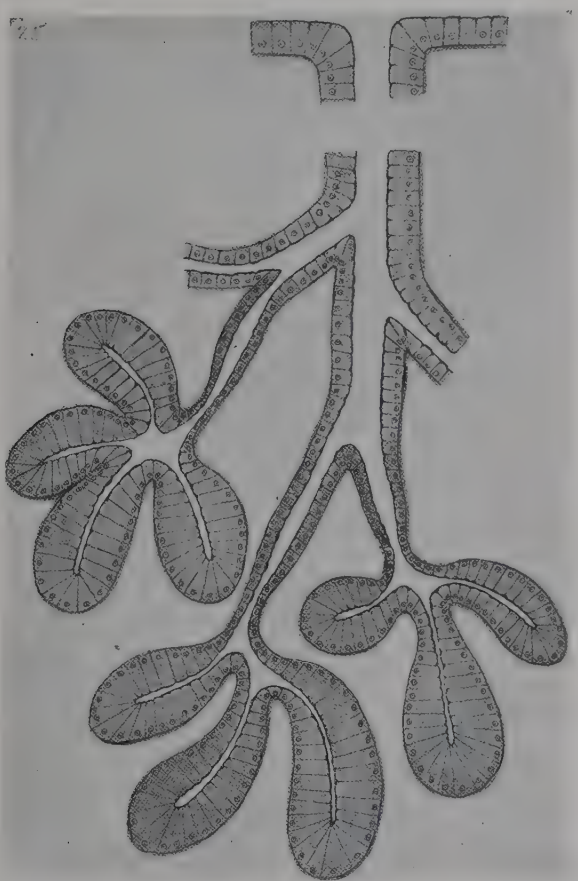


Fig. 25.—Compound Branched Alveotubular Gland. The indifferent parts of the epithelium are bright, the secretory parts are rather darker (schematic).

separated from the tubule by a short, indifferent, intermediate portion. This structure is common to all mucous glands, the large glands of the mouth (Pl. 48, Figs. 115 and 116), Brunner's glands of the duodenum, and the prostate. The lungs also may be regarded as a compound branched alveotubular gland (Pl. 58, Fig. 137).

Closed and Solid Glands

The only **closed gland** in the human body is the thyroid, in which we have roundish or oblong glandular alveoli lined with secretory epithelium, the so-

called **follicles.** The secretion is thrown out into the cavity of the alveolus, and probably is emptied through apertures in the epithelium into the surrounding lymph spaces, when the follicle collapses (Pl. 40, Fig. 100).

There is no cavity to contain secretion in the **solid glands.** The secretory epithelium forms trabeculæ with cell lying close to cell, so that quite a number appear to be grouped in a section of a trabecula. These epithelial trabeculæ may run in various directions in different cases, and have a varying arrangement in the gland, but, as a rule, they unite to form a network. In the meshes of this network lie the blood vessels, with which these glands are always abundantly supplied, that dispose of the secretion. Here belong the parathyroid glands, the suprarenal capsules, and the hypophysis (Pl. 41, Figs. 101 and 102).

Now that we have learned to recognize and to classify glands in this manner from their outer forms, it is necessary to go rather more minutely into their finer construction and their functions. We shall consider only the epithelium, for the description of the less important accessory structures, such as the membrana propria, connective tissue, muscular tissue, etc., appertains to the special microscopic anatomy of the organ concerned.

The duty of secretory glandular cells is either to elaborate in their own bodies certain substances from the materials brought to them by the blood, and to empty such products into their cavities, or to extract these substances already prepared from the blood and then simply to excrete them. Thus urea and uric acid, the two most important constituents of the urine, are not elaborated by the secretory cells of the kidney, but are products of the disintegration of albuminoids in other cells of the body, and are simply excreted by the renal epithelium. But the secretions of most glands are elaborated in their glandular cells, where the process of formation may be followed under the microscope. The preliminary steps of secretion frequently appear in the glandular cells as ***granules,*** and it is now evident that the formation of the latter starts from the ***microsomes*** lying in the protoplasm. These living microsomes take up matter from the material brought to them and elaborate it in a certain way within their own bodies. Consequently they increase in size, change their locations, and finally appear as dead granules of secretion in the meshes of the protoplasm.

In addition to this taking up and elaboration of albuminoid substances, the ***absorption of water*** by the glandular cell is an important factor. This process runs parallel with the other, but we do not know as yet how it takes place, or whether it is through the mediation of special organs, the filamentous structures of the proximal part of the glandular cell, as has been claimed.

The question of the *involvement of the nucleus in the process of secretion* is the subject of much discussion. As has been mentioned already, certain alterations may be perceived in the nucleus during the various phases of the process. While the nucleus lies near the center of the resting cell, which contains no secretion, it moves gradually toward the base as the cell fills with the primordial particles of secretion, until it comes into such close apposition that it can be discerned only with difficulty. Coincidently with this change of location a diminution of its volume usually takes place. The chromatin becomes compressed into a smaller space, so that the nucleus of a cell full of secretion

stains more strongly and looks more compact than that of a cell not thus filled. This reduction of volume may be regular or irregular; in the former case the nucleus preserves its spherical shape, in the latter it becomes greatly deformed and presents dentations and projections, as may be seen very distinctly in the nucleus of the mucous cell.

These visible changes make it probable that the nucleus takes an active part in the process of secretion, and that it furnishes secretory material, but nothing is positively known concerning this. It has been claimed that in certain glandular cells the nucleolus escapes from the nucleus during secretion and disappears in the cell body.

The secretion is emptied from the free surface of the glandular cell into the glandular cavity either directly, or through minute diverticula of the latter, which are called **secretory capillaries.** These are of two kinds, the ***intercellular*** and the ***intracellular.*** **Intercellular secretory capillaries** are minute tubules which follow a straight or slightly curved course between any two cells and have blind ends in front of the membrana propria. They may also be forked (Pl. 48, Fig. 115). Such intercellular secretory capillaries are found in all of the salivary glands, the liver, the pancreas, the pylorus glands, the lacrimal gland, etc. The **intracellular secretory capillaries** extend from the lumen of the gland into the bodies of the glandular cells, or enter the latter as extensions or lateral branches of the intercellular variety. Within the cell bodies they either end in cul de sacs, or they form an intracellular system of canals by branching and anastomosis (Pl. 50, Fig. 120); we find examples of the former in the cells of the liver, of the latter in certain cells of the fundus glands of the stomach.

Although glandular cells, like all others, have only a limited length of life, and we therefore meet with dead ones from time to time, yet they are not destroyed by the process of secretion itself. There is only one known exception to this rule; in the sebaceous glands the glandular cells perish, the nuclei and cell bodies break down and are cast off as constituents of the secretion.

MUSCULAR TISSUE

Every appreciable movement of the human body, or of any of its parts, depends on the existence of a special, muscular tissue, the greatest part of which by far is derived from the mesoblast. The tissue is composed of specific **muscle cells,** which shorten by contraction in response to stimuli and are able to do so because of the presence of certain differentiation products of their bodies, the **contractile fibrils,** protoplasmic threads of varying thickness that run approximately parallel through the length of the cell body. The result of this arrangement is that the shortening brought about by the contraction of all the fibrils in a cell always takes place in only one direction.

The contractile fibrils develop from the protoplasm of the embryonal muscle cell and the formations known to us as mitochondria. The greater part of the cell protoplasm is used for this purpose, the balance, known as **sarcoplasm,** lies in the perfect muscle cell as indifferent protoplasm and envelops the fibrils.

We distinguish two kinds of muscles in the human body, the ***involuntary*** or ***organic,*** and the ***voluntary*** or ***animal;*** the former independent of the will, the latter subject to it. These two kinds of muscle differ essentially in the construction of their contractile fibrils. They are homogeneous throughout their entire length in involuntary muscles, which are also called **smooth muscles** because of this fact. In the voluntary muscles, on the contrary, they are composed of substances of unequal refractive power, which give the cells a transversely striated appearance. Voluntary muscles consequently are also called **striated muscles.**

The **muscle of the heart** occupies an intermediate position between these two varieties, as it is not subservient to the will, and yet its cells contain transversely striated fibrils.

Smooth muscle fibrils are found throughout the animal kingdom, but striated fibrils are absent in the lowest animals. They gradually appear as the scale of life rises, and reach their highest development in the arthropods and vertebrates.

Smooth Muscular Tissue

Smooth muscular tissue is found chiefly in the interior of the human body in the form of continuous membranes in the walls of the hollow digestive, respiratory, and genitourinary organs, where it takes charge of the onward movement of the chyme, the expulsion of foreign bodies, or of epithelial secretions that act as such, the evacuation of the urine, and the ejection of the genital products. It forms a very important constituent of the vascular system, and is also found in the skin and within the eye.

Smooth muscle cells are long, thin, spindle-shaped, or frequently ribbon-

shaped, thickest in the middle and tapering into points at each end (Pl. 23, Fig. 59). Their length varies from 40 to 500 μ, their greatest transverse diameter from 5 to 10 μ. In a cross section the cells usually appear to be roundish, polygonal with rounded corners, or oval (Pl. 23, Fig. 60).

The body of the smooth muscle cell usually has a longitudinal striation, though this is often very indistinct, due to the presence of the **contractile fibrils,** which are divided into the ***internal*** and the ***limiting.*** The latter form a single layer in the periphery of the cell and may be distinguished by their somewhat greater thickness from the internal fibrils, which fill the interior of the cell, where they may either be very compact or lie more loosely. All of these fibrils run parallel through the length of the cell, but whether they become more and more slender as the ends of the cell taper into points, or the outer fibrils terminate sooner than the inner ones, is not yet certain.

Between the fibrils lies unchanged protoplasm, the **sarcoplasm,** containing varying quantities of fine granules. The sarcoplasm also forms a cortical layer over the outer fibrils, known as the **sarcolemma,** in which larger granules are to be found (Pl. 22, Fig. 57).

Each smooth muscle cell contains a **nucleus,** which is always situated near its center where it produces a marked swelling. It is usually cylindrical, or drawn out still more like a rod, and frequently does not occupy exactly the longitudinal axis of the cell, but seems to be somewhat hollowed toward the latter. In the depression thus formed lie two little **central corpuscles.** Both the cell body and the nucleus undergo great changes of shape during contraction. The contractile fibrils become much thickened at certain places, called **contraction nodes,** where the individual fibrils draw close together and seem to blend. Dark lines are formed in the stained specimen which run transversely or obliquely over the cell.

Smooth muscular tissue is formed from these smooth fibers lying close together. No such protoplasmic cell bridges are to be found as are often to be seen in epithelial tissue, but the fibers are held together by connective tissue with a small quantity of cement. The cells may be assembled to form bundles which may either lie parallel and unite to form muscular coats, or may interlace and decussate (Pl. 22, Figs. 57 and 58).

Striated Muscular Tissue

Striated muscular tissue is perhaps the most important of all the tissues in the construction of the human body. The muscles composed of it form over 40 per cent. of the body weight. They comprise all of the motor muscles of the trunk, head and limbs, the so-called skeletal muscles, those of the upper part of the alimentary and respiratory tract, i.e., of the mouth, tongue, pharynx, larynx, and the upper two thirds of the œsophagus, and those of the orbit, the tympanum, the external genital organs, and the anus.

The cells that compose this tissue, the **striated muscle cells,** differ essentially from those of the smooth muscles that have just been described; they are much larger, are of a different shape, have striated instead of smooth fibrils, and contain many nuclei instead of a single one.

The form of a striated muscle cell is that of a very long prism, the edges of which are more or less rounded off. Consequently, it presents on cross section the picture of a polygon with rounded corners, and on longitudinal section a band so long that it is very seldom seen throughout its entire length (Pl. 25, Figs. 63, 64 and 65). For this reason it is commonly spoken of as a **striated muscle fiber,** but we must always bear in mind that it is only a single cell, no matter how extreme its length may be.

The diameter of the striated muscle fiber is about the same throughout its course, except that each end tapers to a blunt point, and is considerably greater on the average than that of the smooth muscle cell. Although striated muscle fibers are to be found that are only 10 μ thick, or even thinner, the great bulk of them range in thickness up to 100 μ, but this maximum is never exceeded. The thickness depends in the first place on the age of the individual, as it increases from birth until growth is complete, and in the second place on the size of the muscle and the degree to which it has been developed. Large muscles and robust persons have larger fibers than small muscles and weakly individuals. The length also is very variable, as it depends on the length of the muscle to which it belongs. We know that they run the entire length of small muscles, but it is difficult to determine whether this is the case in long muscles or not, though fibers over 10 cm. long have been isolated from them.

Irregular forms of muscular fibers are not uncommon. Thus we find in the tongue and in the ocular muscles fibers that split into many small branches, **branched muscle fibers.** We meet with such branched fibers in the *muscle spindle* also, but here the branches reunite and give rise to a **muscular network** (Pl. 68, Fig. 160).

As in the smooth muscle cells, the *contractile fibrils* form the most essential constituents of the striated muscle fiber, and in addition we have in each the *sarcoplasm,* the *sarcolemma,* and the *nuclei.* Central bodies have not been found.

The **contractile fibrils** occupy the entire length of the body of the muscle fiber, and are commonly packed very closely together. We suppose, for positive proof can hardly be obtained, that each contractile fibril runs the length of the fiber to which it belongs. The fibrils are round threads 2 μ thick, and, if we isolate them by means of suitable chemical agents, they present structural bands of light and dark segments that alternate regularly, the brighter bands being the broader. If we move the micrometer screw during the observation the picture changes, the light bands becoming dark, the dark ones light. This phenomenon shows that we have to deal with two substances of different refractive power. With the aid of the polariscopic microscope the broad bands between the crossed Nicol prisms attain their maximal brightness and darkness four times during a rotation of 360°, and are therefore **doubly refractive,** or **anisotropic,** while the narrow bands are equally refractive in all directions, are **singly refractive,** or **isotropic.** Hence in every fibril broad anisotropic bands, marked as Q, alternate regularly with narrow isotropic bands marked as I. Each anisotropic band is further divided into two halves by a narrow isotropic stripe (h), and likewise each isotropic band by a narrow anisotropic stripe (Z). Starting with Z we have the following regular order

of rotation: Z, I, Q, h, Q, I, Z, I, Q, h, Q, I, Z, etc. We designate any segment of a fibril lying between two Zs as a **muscular compartment,** i.e., the individual muscular compartments are separated by the narrow anisotropic Z stripes, or intermediate discs.

When the fibril contracts the picture changes and becomes simpler. The **contraction** passes like a wave over the fibril, which becomes shorter and thicker. The thickening affects the anisotropic segments, while the isotropic on the contrary become smaller, so that the former blend, and we have the broad, doubly refracting bands forming a simpler alternation with the narrow singly refracting ones. But the refractive conditions also have changed; the two substances have approximated in their refractive powers and consequently are no longer to be so sharply distinguished from each other.

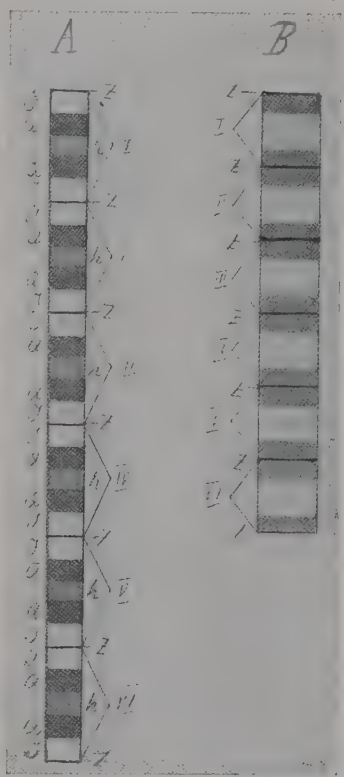


Fig. 26.—Transverse Striation of a Muscular Fibril. *A*, during rest; *B*, during contraction.

While the contractile fibrils lie parallel in the muscle fiber they are arranged at the same time so that the corresponding bands all lie at the same level and run across the entire fiber without interruption. We may therefore speak of them as **discs** placed one after another in the fiber (Pl. 27, Fig. 70).

We may break down the fiber into **discs** by means of certain chemical agents that cause the individual parts to swell, or to shrivel. The fiber then falls apart into separate pieces, like a roll of coins, but these pieces never correspond to a single muscular compartment. The intermediate discs that separate the compartments are extremely resistant, and the separation takes place either in the middle disc (h), or within the isotropic disc I.

We will now consider more minutely the arrangement of the contractile fibrils within the muscle fibers. On cross section the fiber exhibits more or less distinctly a network with fairly fine, irregularly triangular, quadrangular, or polygonal meshes, which blends at the periphery with an outline surrounding the fiber. This picture we call **Cohnheim's fields** (Pls. 24-27). We learn from corresponding longitudinal sections that Cohnheim's fields are the cross sections of the contractile substance, which is placed in the form of long prisms in the muscle fiber. These prisms are the **muscle columns,** and are composed of the contractile fibrils. The diameter of Cohnheim's fields, or of the muscle columns, may be said to be about 5 μ, differing in different muscles, but approximately the same in any one. That of the fibril, on the contrary, appears to be fairly invariable, so a muscle column is composed of fewer contractile fibrils in one muscle than in another.

Another important constituent of the striated muscle fiber is the **sar-**

coplasm. This appears in the living or surviving muscle fiber as a homogeneous, or very indistinctly granular mass, which, while fresh, stains strongly with hæmatoxylin. The contractile substance remains almost wholly unstained, so the sarcoplasm can be brought out in this way very plainly. It is this that makes Cohnheim's fields prominent in the cross section of a muscle fiber, as it separates the muscle columns from one another (Pls. 25-26). Cohnheim's fields are the cross sections of the muscle columns; the network that separates them and forms longitudinal partitions that unite laterally to create long tubes in the muscle fiber, is the sarcoplasm.

It is extremely difficult to preserve the sarcoplasm. Most of our preservatives cause it to swell and destroy it, while they save the muscle columns. For this reason the picture presented by the cross section of a preserved muscle fiber differs materially from that of a fresh one. The very regular division into fields in the latter is replaced by one which is very irregular, because the swelling of the sarcoplasm produces large, communicating spaces, between which lie muscle columns blended irregularly into fields of contractile substance. Hence the cross section of the preserved fiber does not present the true Cohnheim's fields.

The septa of sarcoplasm are not so thin and delicate, or so regularly arranged and joined together in all muscle fibers as would appear from the above description. In some places they are thicker and more irregular, especially where three meet and bring together a larger mass of sarcoplasm (Pl. 25, Fig. 65). As such fibers are usually more slender, and have a smaller cross section than others, the amount of sarcoplasm in them may be equal, or even greater than that of the contractile substance. Such fibers are said to be ***rich in sarcoplasm,*** or ***cloudy.*** They are found in man in muscles that are constantly active and make very quick movements, such as those of the eye. The fibers of the skeletal muscles have the structure previously described, and are said to be ***poor in sarcoplasm, clear muscle fibers.***

Sarcoplasm is divided into hyaloplasm and granoplasm, the same as any other protoplasm. It also contains granular formations which, taken together, forms the **interstitial substance** of the muscle fiber. Generally speaking we may say that muscle fibers rich in sarcoplasm appear to be richer in interstitial granules than those that are poor in sarcoplasm. The granules lie chiefly at the points of junction of the network of Cohnheim's fields, and therefore run in parallel courses through the fiber (Pl. 26, Fig. 68). They are most numerous at the periphery. We learn from longitudinal sections that these granules are deposited at the level of either the isotropic disc I, or of the anisotropic disc Q, and we call them accordingly I or Q granules.

Various substances take part in the chemical composition of the interstitial granules. The first of these to be mentioned is **fat,** which occurs in very variable quantities in the muscle fibers, the content depending to a great degree on the nutritive condition of the individual. There are some interstitial granules that consist wholly of fat, and others in which a nucleus of fat is enveloped in material that is soluble in water. This may be seen very beautifully when we treat a fresh section of muscle with distilled water; the enveloping substance is dissolved and the previously invisible fat granules come into view (Pl. 24, Fig. 64). Another important component of the interstitial granules is **glycogen.**

Some granules consist wholly of this substance, and it may be that it forms the soluble envelopes which have just been described. **Lecithin** also takes part in the composition of the interstitial granules.

The sarcoplasmic septa unite at the periphery of the muscle fiber to form an outer covering called the **sarcolemma** (Pls. 24-26). Thus the conditions here are the same as in every other cell of the body, for the sarcolemma is in fact a specific membrane. If we isolate fresh muscle fibers and place them in distilled water, the water will destroy both the contractile substance and the sarcoplasm, leaving the sarcolemma perceptible, at least in places, as an empty tube. This is not contradictory of what has been said above. We must consider the sarcolemma as intermediate between the crusta and the pellicle of the cell; like the one it passes over immediately into the sarcoplasm, while it has the firm consistence and greater power of resistance of the other.

The last constituent of the muscle fiber remaining to be discussed is the **nucleus.** Each muscle fiber originates from a cylindrical cell of the myotome of the embryonal body, which contains a single nucleus, but as it increases in length indirect segmentation takes place continuously in the nucleus so that finally the fiber when completed is a polynucleated cell. The number of nuclei varies; the thin fibers contain more on an average than the thick, but the number depends greatly on the length of the fiber, very long ones having hundreds.

In man the nuclei almost always lie peripherally, just beneath the sarcolemma, and have their inner sides covered by a small quantity of sarcoplasm, but in certain muscle fibers, as in those rich in sarcoplasm, they are most frequently removed from the sarcolemma and lie embedded in sarcoplasm between the muscle columns. This is likewise the condition in the so-called **red muscles.** The very marked redness of certain muscles is attributable in the first place to the richness of their vascular supply, in the second place to the amount of hæmoglobin, or of its derivative myohæmatin, dissolved in the sarcoplasm of their fibers. The peripheral position of the nuclei is characteristic of the muscles of man and of animals; in all other vertebrates they are distributed uniformly in both the internal and peripheral layers of the fibers (Pl. 26, Figs. 67 and 68).

The nuclei of the muscle fiber are ellipsoidal in shape, frequently have an irregular, uneven surface, are rich in chromatin, and usually contain several nucleoli.

As is well known, the muscles of a grown man may be enlarged considerably by good nutrition and suitable exercise. This enlargement is due primarily to a stoutening of each individual muscle fiber, not by an increase in the size of the individual fibrils, but by a multiplication of their number through longitudinal division. The nuclei arrange themselves in several longitudinal rows, between which the division takes place.

In the branched muscle fibers, found in the tongue and in the muscle spindles, the conditions are quite similar to those in the simple fibers. The fibrils pass from the thicker trunk into the more slender branch without splitting or branching themselves, and so follow uninterrupted courses throughout the entire fiber.

The Cardiac Muscle Fiber

The branched striated muscle fibers lead us to those of the muscle of the heart. Although it is very rarely that striated muscle fibers in general split, branch, anastomose, and form networks, this behavior is a characteristic of those of the cardiac muscle, in which all of the fibers branch dichotomously as a rule in every plane. By the junction of these branches the musculature of the heart forms a very extensive **muscular network** that has exactly the same components as the fibers of the skeletal muscles, contractile fibrils, sarcoplasm with interstitial granules, sarcolemma, and nuclei (Pl. 28, Fig. 71).

The **fibrils** course without interruption through the fibers, and it is improbable that they split or branch. They are ***transversely striated*** throughout their entire length and show the same alternation of isotropic and anisotropic substances as those of the fibers of the skeletal muscles, from which they differ in only one essential point. The striation appears to be broken at certain places and the fibrils to be homogeneous for a little way, as though a short rod had been interposed in the course of the fibril. These places are spoken of as **interpolated sections.** The interpolated sections of the adjoining fibrils may lie together so as to form a plate across the fiber, or they may be at slightly different levels so as to create a picture that resembles a flight of steps, whence they are called **cement striæ,** or **stairs** (Pl. 28, Fig. 71). The stairs may pass through the entire thickness of the fiber, or through only a part of it; in the first case all of the fibrils are broken, in the latter only a part of them are interrupted.

There has been much discussion concerning the nature of these stairs. Some hold them to be contraction phenomena of the fibrils which take place during the death of the fiber, and to be to a certain degree **artefacts.** Others believe them to be preexisting formations of functional importance, either a sort of **intervening tendons,** or of **accretion lines** from which the growth of the fiber proceeds. Finally they have been taken to be **limiting cell lines,** and have been called cement lines, as they are composed of a special cement substance. By treating the cardiac muscle with strong liquor potassæ the fibers can be broken into segments that have these stairs at their ends and contain a variable number of nuclei. According to this theory the cardiac muscle is composed of roughly prismatic cells that send out short, likewise prismatic processes in all directions, which join the separate cells and so produce the apparently fibrous network.

The fibers of the human cardiac muscle also differ materially from those of the skeletal muscles in the arrangement of the contractile fibrils. Instead of forming regular, prismatic muscle columns, the fibrils unite into **irregular leaves,** which converge from the periphery toward the axis of the fiber. The individual leaves may split and join together. The axis of the fiber is quite free from fibrils (Pl. 28, Fig. 73, c).

The interspaces between the leaves of fibrils are filled with **sarcoplasm,** which forms similar, though decidedly narrower leaves (Pl. 28, Fig. 73, a). The finer points of structure are the same as those of the skeletal muscle fibers. Fresh hyaline protoplasm contains many **interstitial granules** that have the

same composition as in those fibers (Pl. 28, Fig. 73, b), and are commonly very fine. The isotropic and anisotropic substances of the contractile fibrils are also disposed in the same typical manner.

The leaves of sarcoplasm start at the periphery from a **sarcolemma** (Pl. 28, Fig. 73, a).

The **nuclei** always lie about the axis, surrounded by a small quantity of sarcoplasm. The latter is usually so little that the leaves of fibrils seem to reach the membrane of the nucleus, and the leaves of sarcoplasm to start directly from the latter. The light areolæ that appear to surround the nuclei in the fixed specimen are artefacts caused by the shrinkage of the leaves of fibrils and the swelling of the sarcoplasm, just as they are formed in the skeletal muscle fibers (Pl. 28, Fig. 73, a and b).

Just as the same structure is not present in all true striated muscle fibers, so there are marked differences in fibers from different parts of the heart. The structure above described is common to the great mass of the musculature of the auricles, ventricles, and papillæ, but we find other conditions in the cardiac muscle system that joins the auricles and ventricles, starting from the valvular sinus coronarii of the right ventricle and extending to the ventricular septum, a system of great functional importance and known as the **bundle of His.** In man the fibers here are thicker and much richer in sarcoplasm than those of the ordinary cardiac muscle, the fibrils also are thicker and do not lie so closely together, and the interstitial granules are more numerous and more dense. In hoofed animals and other large mammals these fibers can be seen even more plainly, first, because of their thickness; second, because the fibrils form a peripheral mantle, as in the embryonal muscle fiber, while the interior contains simply sarcoplasm and nuclei. These fibers are named after their discoverer **Purkinje's fibers.**

Nervous Tissue

Although the power to conduct stimuli is common, to a certain degree, to the protoplasm of every living cell, yet it is possessed κατ ἐξοχήν by the nervous tissue. Every external stimulus that falls upon our bodies is received by either this tissue itself, or by special perceptive cells, and transmitted to the central nervous system where it is elaborated. Special fibrils are differentiated from the protoplasm of the cells that make up nervous tissue, just as in the muscle cells; we call these **neurofibrils,** and we ascribe to them the special conduction of stimuli.

The great majority of nerve cells lie in the central nervous system, the **brain and spinal cord,** or in peripheral masses of varying size called **ganglia.** Isolated nerve cells are met with much more rarely.

Muscle cells have a certain uniformity of shape and appearance, but this is entirely lacking in nerve cells, as might be expected from the multiform duties they are called upon to perform. In order to conduct stimulus from the periphery to a central organ, elaborate it, and transmit it to a muscle fiber, they have to develop many long offshoots that connect all of these places.

These offshoots are of two kinds, the **neurites** and the **dendrites.** The former are usually single, while more than one of the latter commonly emanate

from the cell body. The neurite may pass through the central organ as a single unbranched process for a long distance, or it may run from the organ to the periphery. It usually has a sheath, and this combination of a neurite

Fig. 27.—Schematic Representation of a Motor Neuron.

a, neurite; *b*, dendrite; *c*, nucleus of the nerve cell; *d*, tigroid substance; *e*, neurofibrils radiating from the cell body into the neurites; *f*, collaterals; *g*, axis cylinder of the nerve fiber which leaves the central nervous system at *h*; *i*, cylindroconical medullary segments; *k*, Ranvier's constrictions with cement discs; *l*, Schwann's sheath with Schwann's nuclei; *m*, muscular fiber in which the axis cylinder ends at *n* in an antlered formation.

with its sheath is what we call a **nerve fiber.** Dendrites likewise may become nerve fibers, so that in certain cases two fibers may develop from one nerve cell, but, as a rule, the dendrites do not attain such great length as the neurites, and do not leave the central organ.

It is evident from the above that, although these extremely long nerve fibers are integrant parts of the cells, they acquire a certain independence, enough so that we may consider nervous tissue to be composed of **nerve cells** and **nerve fibers.** The nerve cell with the dendrites and the nerve fiber coming from it form the nerve unit, the **neuron.**

In addition to these specific cells and fibers, nervous tissue contains other elements that have the same origin, but play the more subordinate part of filling and supporting material. These are the branched glia cells, from the bodies of which **glia fibers** extend in a manner similar to that seen in connective substances, which we shall study later. **Glia tissue,** formed of glia cells and glia fibers, we therefore regard as a supplement to nervous tissue.

Nerve Cells

Nerve cells vary a great deal in shape, but may be said to have three fundamental forms, spherical, spindle-shaped, and polyhedral, between which every possible transition may be found. The shape of the cell is influenced very materially by the number of its processes, and we distinguish accordingly as they have one, two, or more ***unipolar, bipolar,*** and ***multipolar cells.***

Unipolar cells occur preeminently in the spinal ganglia and in those of the cranial nerves, the Gasserian, the geniculate, the superior and inferior of the pneumogastric nerve, the petrosal, and the jugular, where they often have the shape of a pear, or of an egg. A fairly thick process comes from the cell, curls closely about its body in numerous convolutions, and then starts off in a straight course (Pl. 29, Fig. 74; Pl. 83, Fig. 182). At a greater or less distance from the cell it splits into two branches, one of which goes to the periphery as a sensory nerve fiber, while the other enters the spinal cord as a fiber of its posterior root. We may call the former a dendrite, the latter a neurite. In embryonal life the cell has two processes instead of one, but as development proceeds the two draw near together and finally blend at the place where they leave the cell. In the lowest vertebrates, the fishes, the cells maintain this embryonal condition throughout life.

Bipolar cells occur in the vestibular and spiral ganglia of the auditory nerve. The generally roundish cell body is pointed at each end, from which it sends processes, one to the sensory epithelium of the ear, the other to the brain as a fiber of the auditory nerve. Here also we may call the former a dendrite, the latter a neurite (Pl. 29, Fig. 75).

The great majority of nerve cells are **multipolar.** They vary extremely in shape, but may be said to belong to two types, one of which is denominated the ***motor,*** the other the ***sensory,*** with every possible transition between them.

The **motor cell** has a large, polyhedral cell body from which processes radiate in all directions (Pl. 29, Fig. 76; Pl. 79, Fig. 176, vwz; Pl. 81, Fig. 178, vwz). These processes usually start from the cell body with a fairly broad base, taper gradually, continuously divide dichotomously, attain a very considerable length, and terminate in quite fine points. These are the dendrites. In comparison with them the origin of the neurite, which is always single, is very difficult of detection. The neurite arises from a conical elevation of the cell

body as a very delicate, slender thread, which first assumes a considerable caliber at a little distance from the cell, and then remains of the same size for the rest of its course. Together with its sheath it becomes a nerve fiber, which is never the case with the dendrites of the motor cell.

Very rarely a neurite behaves differently, and suddenly splits up into a large number of very fine fibrils soon after it leaves the cell. Such cells are said to be of ***Golgi's type,*** while those that behave in the ordinary manner are said to be of ***Deiter's type.***

The **sensory cell** is characterized by an elongated body, which may be of a perfect spindle shape in typical cases (Pl. 79, Fig. 176, coz, hhz; Pl. 81, Fig. 178, coz). The dendrites come from the two poles of the cell body, and may be extremely long, but are never as stout at their origin as those of the motor cell. The neurite behaves similarly to that of the motor cell, coming from either the cell body itself, or from one of the dendrites. As said above, many transitional forms exist between these two types, and we often find it difficult to determine from its shape alone, in an individual case, whether a cell belongs to the one or the other.

Another peculiarity of the neurites of both motor and sensory cells is the possession of **collaterals.** By this term we understand fine, lateral twigs that usually leave the neurite at a right angle and split up into terminal filaments after a relatively short course. They end within the central organ, or a ganglion, and during its course through the central organ a neurite may give off a very large number of such collaterals.

Neurites terminate in many ways. Motor neurites end in all of the muscle fibers in the form of motor end plates (Pl. 70, Fig. 162). Other neurites split up at their ends and form fiber baskets, or clawlike end organs, with which they embrace other nerve cells, while still others branch and twine as it were with their twigs about the bodies and dendrites of other nerve cells.

The **structure** of the nerve cell also offers much of interest. As stated at the beginning of this chapter, the **neurofibrils** form their most essential component. Like contractile fibrils they are differentiations of the cell protoplasm. They are absent from the nerve cells in the early stages of embryonal life, but gradually develop in the cell bodies and extend out into the processes of the latter. They resemble contractile fibrils in being smooth threads, but differ from them in always being uniformly isotropic throughout their entire length. They have slight refractive power and are therefore comparatively difficult to detect when not stained. They are considerably more slender than contractile fibrils on an average, yet stout ones are found together with others that are very slender, and many observations go to show that their bulk changes with the functional condition of the cell.

The neurofibril is also a much more labile structure than the contractile fibril, and undergoes marked changes very soon after death, becoming first like a string of pearls, and later breaking down into clear granules. Most observers describe these fibrils as solid, but some believe them to be hollow tubes that contain fluid.

Another essential point of difference between the neurofibrils and contractile fibrils is that the former branch and form networks.

Neurofibrils are oxyphilic, like contractile fibrils, but are very difficult to stain by our ordinary methods.

The manner in which the neurofibrils are arranged in the body of the nerve cell is very inconstant. They are never distributed quite uniformly, but radiate into it in bundles from the neurites and dendrites. The bundles of fibrils either simply traverse the body of the cell from the neurite to the dendrites, or from one dendrite to another, or they form a network within the body from which other bundles of fibrils are collected and sent off (Pl. 30, Fig. 77). These fibrillary nets lie either in the superficial parts of the cell body, or pressed close to the nucleus. Both sorts may be found in the same cell, and are then joined by bands of fibrils.

Fig. 28.—Motor Nerve Cell of the Spinal Cord (semischematic).
a, dendrites; *b*, neurite; *c*, neuroplasm; *d*, tigroid substance; *e*, neurofibrils; *f*, pigment.

In the neurite the neurofibrils at first lie very close together, but farther along they loosen up somewhat and form the **axis cylinder** of the nerve fiber, which will be described later. In the dendrites they are packed less closely. Wherever a dendrite branches the fibrils usually form little nets.

The neurofibrils lie embedded in neuroplasm, which corresponds to the sarcoplasm of the muscle cells. It is not always easy to demonstrate this

substance, but it often shows an exquisite vacuolized structure, in which the vacuoles are very fine, and have the neurofibrils running in their walls.

The nerve cell contains a third component which is more striking to the eye in a properly killed cell, and can be stained much more easily than either of the others, the **tigroid substance.** The bodies of living or surviving nerve cells show an almost homogeneous appearance, with at most, at least in many cases, indications of the neurofibrils to be seen within it. Yet if fixing reagents that precipitate albumin are used to preserve and stain it, the picture changes at once and the cell becomes mottled. This is due to the appearance within the cell body of flakelike deposits, which are known under the names of **tigroid substance,** and **Nissl's clods,** or **granules** (Pl. 31, Fig. 78).

These bodies vary a great deal in appearance. In the large motor cells they form irregular, angular, or roundish bodies of conspicuous size, which often exceed in dimensions the large nucleolus of the nerve cell. Smaller cells frequently contain very few large flakes, while in the cells of the spinal ganglia they are so small and so closely packed as to make the cell look dusty. Their situation also varies; they may form a circle about the nucleus, a **perinuclear ring,** or they may lie wholly in the periphery and form a **marginal areola.** The form and arrangement of the clods are fairly constant for the different varieties of nerve cells and are therefore of great help in distinguishing the latter apart. Clods are to be found not only in the true cell body, but also for a distance in the dendrites, where they have a more elongated, spindle shape. The only parts of the cell that are free from them are the neurite and its cone of origin (Pl. 31, Fig. 78).

When we examine these clods with the highest powers of the microscope we find them to be composed of fine granules, and it can be perceived that they do not form a deutoplasmatic constituent of the walls of the alveolæ of the neuroplasm, but rather a sort of microsome.

These clods of Nissl have so great an affinity for basic dyes that they have been pronounced *basophilic bodies*, but this is only when the conditions described in the chapter on "The Cell" have not been observed correctly, for they take the acid rather than the basic component of a mixture of coloring matters and are therefore oxyphilic. Their chemical reactions are as follows: They are dissolved completely by alkalies, like soda and liquor potassæ; they are partially dissolved by the gastric juice and trypsin; they are precipitated by reagents that precipitate albumin. These reactions indicate that the tigroid contains a complex body, composed of nuclein and a substance resembling globulin.

Among the other structural parts of the body of the nerve cell is the **reticular apparatus,** which is similar to that found in other cells of the body. It forms a relatively wide meshed network of medium sized threads about the nucleus, which may, perhaps, be a system of canals filled with a substance that possesses to a high degree the power to reduce osmium terroxide.

Central bodies do not appear to be present in the adult nerve cell, but they are to be found in the embryo in pairs close to the nucleus.

Another substance very often met with in the body of the human nerve cell is a lipoid, or fatty **pigment.** Usually its granules are very small, of a yellowish or brownish color, and may lie massed together, or be distributed

pretty uniformly. The amount of pigment increases as the person grows older. These pigment holding cells impart a stain, which is macroscopically visible, to many places in the central nervous system, such as the substantia nigra, and the locus cœruleus.

The single **nucleus** of the nerve cell is distinguished by its size. It is almost always globular, and rarely exhibits slight irregular dimples, or indentations (Pl. 31, Fig. 78), but in spindle cells it is commonly ellipsoidal in shape. As a rule its size bears a certain proportion to that of the cell, but there are exceptions in which it is enclosed in a very thin cell body, as in the little granular cells of the cerebellar cortex.

The nucleus of the nerve cell is poor in chromatin in comparison with those of other cells, so that it appears clear and vesicular in the stained specimen. The chromatin forms a chromatic membrane, and also a few particles situated for the most part about the nucleolus. In addition radiating, oxyphilic cords are to be seen running through the nucleus; these are called sometimes oxyphilic chromatin, sometimes linin.

But the most prominent part of the nucleus of the nerve cell is the **nucleolus,** which attains a size met with elsewhere only in the ovum, and is situated more or less exactly in its center. Its staining reaction is not constant; as a rule it is purely oxyphilic, like all other nucleoli, but in many cases it shows a certain affinity for basic dyes. This indicates that it is composed of two different substances, pyrenin and nuclein, or, in the opinion of some authors, pyrenin and plastin. Small granules frequently appear in the nucleolus, and are known as nucleoluli, or corpusculi intranucleolares.

Exceptions to this description are to be met with. Thus the nuclei of the little granular cells of the cerebellar cortex are rich in basophilic chromatin, and this is generally true of all nerve cells in their early stages of development. In the course of development the nucleus becomes poorer in chromatin, and the latter gradually loses its capacity to stain with basic dyes.

The Nerve Fiber

Every nerve fiber originates as an offshoot of a cell situated in either the central nervous system, or a peripheral ganglion. This projection of the cell forms the most important constituent of the fiber, and we designate it as an **axis cylinder.** It forms the only constituent at the place where the fiber starts from the cell, but very soon it becomes surrounded by two structures, the **medullary sheath** and the **sheath of Schwann.** It would be more correct to say that the axis cylinder may become enwrapped by these sheaths, for it may remain entirely naked, may have but one of the two sheaths, or may have both; consequently we may distinguish four different kinds of nerve fibers:

1. ***Those that consist of naked axis cylinders;***
2. ***Those in which the axis cylinder is covered by a medullary sheath;***
3. ***Those in which the axis cylinder is covered by a sheath of Schwann;***
4. ***Those that consist of an axis cylinder, a medullary sheath, and a sheath of Schwann.***

The only nerve fibers that consist of naked axis cylinders throughout are found in the ***olfactory nerve,*** but the axis cylinders of all fibers are naked for a little way at their ***origins,*** as has been mentioned already, and become so again at their ***ends,*** after they have lost their sheaths. These naked initial and end pieces may be pretty long under certain circumstances, as in the intraocular portion of the optic nerve, and in the sensory posterior root fibers in their courses within the gray substance of the spinal cord, but in most cases they are quite short.

Fibers that consist of an axis cylinder and a sheath of Schwann are characteristic of ***sympathetic*** nervous system, and are usually known as **nonmedullated,** or **Remak's fibers.** They are to be found in the ganglia, principal trunk and nerves of the sympathetic system, and also in large numbers in other peripheral nerves.

The fibers of all ***cranial*** and ***spinal nerves*** are composed of axis cylinders encased peripherally in medullary sheaths and sheaths of Schwann.

The **axis cylinder** is therefore the most essential portion of the nerve fiber and is never absent. It is a round cord, varying in diameter from a fraction of a micromillimeter to ten micromillimeters (Pl. 71, Fig. 165), that extends without interruption from the cell in which it originates to the end of the fiber. Its structure also shows it to be a true cell process, for it is composed of the two fundamental parts of the body of the nerve cell, neuroplasm, called here **axoplasm,** and **neurofibrils.** The axoplasm is a semisolid mass of alveolate construction, which is very difficult to demonstrate. The neurofibrils run parallel to one another in the alveolate walls (Pl. 31, Fig. 79), and naturally have the same properties as those of the nerve cell, of which they are direct continuations. Just as in the more slender initial portion that has been described, they are compressed closely at many places in the fiber and perhaps fuse into thicker fibrils.

The **medullary sheath** forms a cylindrical mantle about the axis cylinder which is not continuous, but is broken into ***segments,*** one placed close behind another. The length of these medullary segments depends on the thickness of the fiber; the thicker the fiber, the longer are the segments. When the fiber is very thick they may be nearly a millimeter long. The thickness of the medullary sheath varies, but is always less than that of the axis cylinder, and may be so extremely thin as not to exceed 5 μ. The fiber appears to be constricted between the segments because of the absence of the sheath at these points, forming what are known as **Ranvier's nodes** or **rings,** one of which intervenes between every two segments (Pl. 31, Fig. 79; Pl. 83, Fig. 182; Pl. 84, Fig. 184, mlrf).

Each medullary segment consists of two chemically and physically different substances, **myelin** and **neurokeratin,** which taken together form the **myelin** or **nerve medulla.** Myelin is a very refractive body which forms lumpy masses in water, a property that is also characteristic of lecithin, which forms its chief constituent together with protagon and fat. Neurokeratin on the contrary has only a slight refractive power and resembles keratin chemically. The nerve medulla has the characteristic property, in common with fat, of strongly reducing osmic acid and of holding *chronhæmatoxylin* very firmly.

It exists in the medullary sheath in a semifluid form together with a system of ***firm, supporting fibers,*** which form a superficial, wide meshed network that extends from section to section like a funnel down to the axis cylinder in such a way that each medullary segment in turn consists of quite a number of cylindrical pieces that overlap one another somewhat at their ends. These are called the **cylindo-conical segments** (Pl. 31, Fig. 79).

The ends of every two medullary segments are separated from each other at Ranvier's constrictions by a plate of cement substance that surrounds the axis cylinder, the **intermediate disc.** Like all cement substances it reduces silver salts, so that if a fresh medullated nerve fiber is treated with a solution of silver nitrate a transverse trabeculum appears at this place, and is often crossed by a longitudinal one, forming what is known as **Ranvier's cross.**

The **sheath of Schwann,** or the **neurilemma,** is nucleated, unlike the medullary sheath, and is to be regarded as the matrix of the latter, as the nerve medulla is formed from it, or from the cells of which it is composed. On the fresh nerve fiber it appears as a quite pale outline external to the medullary sheath and broken like it by Ranvier's nodes, while firmly adherent to the intermediate discs. In general it is structureless, but a granular protoplasm can be seen in many places, which is massed somewhat about the nucleus. Each nucleus in the human sheath always corresponds to a medullary segment, so that we may also speak of the nucleated segments of the sheath of Schwann (Pl. 31, Fig. 79; Pl. 71, Fig. 165).

Glia Tissue

Although nerve and glia tissue have exactly the same origin they develop in quite different directions. While the one develops into a typical stimulus, conducting and elaborating tissue, the other assumes rather the type of connective substance, as shown by the fact that its cells compose a fibrous substance, although lacking in its independence. Glia tissue consists of **glia cells** and **glia fibers.**

Glia tissue is also known as **neuroglia.** It is found outside of the central nervous system only in the optic nerve. It serves as a supporting and filling substance and is perhaps of value in the isolation of nerve conduction.

Glia cells present two modifications,—the ***ependymal cells*** and the ***astrocytes.*** The ependymal cells form the epithelial covering of the system of cavities found in the central nervous system, lining the central canal of the spinal cord and the ventricles of the brain, yet undergo a sweeping reduction in adults. In young persons they form a single layer of cylindrical or cuboidal cells, the free surfaces of which look into the ventricles, or the central canal, and are provided with cilia. At their opposite ends they taper into processes that extend for longer or shorter distances into the brain or spinal cord (Pl. 80, Fig. 177, ep).

The **astrocytes,** on the contrary, are to be found everywhere in the central nervous system scattered about amongst the true nerve cells and forming masses of glia in many places. Their special relations will be discussed later in the description of the central nervous system (Pl. 80, Fig. 177, glz).

The astrocytes are, as their name implies, for the most part branched, stellate cells with small bodies and many processes. The latter either may radiate from the body in all directions, or may have a more polar arrangement when the cells are more spindle-shaped. In man the astrocytes usually contain several nuclei, which vary a great deal in appearance, and are often lobulated, hour-glass shaped, or perforated. They differ from the nuclei of the nerve cells by being smaller, and by appearing darker than those clear, vesicular nuclei when ordinary staining methods are employed, because they are always fairly rich in basophilic chromatin.

Glia fibers are uniform threads of greater or less thickness and often of extraordinary length. They originate in the bodies of the astrocytes and, when fully developed, run through these bodies and their offshoots in such a way that they may be said to be intracellular for at least a large part of their course. Probably this is not true of all glia fibers; it is more likely that some of them may dissociate themselves completely from their cells of origin and become independent. The substance of the glia fibers is not the same as that of the protoplasm of the astrocytes, of which the fibers are differentiation products.

These glia fibers envelop the central nerve cells with networks, wind everywhere between the central nerve fibers, for a sort of external limiting membrane on the outer surface of the central organ, and develop similar membranes that separate all of the vessels of the central nervous system from the nerve tissue.

The Development of Nervous Tissue

It may be well to glance briefly over the histogenesis of nervous tissue in order that we may understand better its construction.

The entire nervous tissue of the human body originates from an invagination of the ectoderm, the neural canal, the wall of which consists, at its end, of several layers of ovoid and cylindrical cells. These are at first absolutely undifferentiated embryonal cells, but very soon they begin to develop in two different directions and to form **neuroblasts** and **spongioblasts.** The neuroblasts may be identified at an early stage by the fact that neurofibrils with a netlike arrangement develop in their bodies, advance peripherally in the direction of the principal axis of the cell, and form the axis cylinder process or neurite. The dendrites develop later from the body of the neuroblast, which thereupon becomes a nerve cell.

The spongioblasts are the mother cells of the glia tissue. They are cylindrical, originally reach from the lumen of the neural canal to the so-called marginal film, and likewise give off many processes. Part of them gradually draw back from the inner surface of the neural canal and come to lie with their cell bodies between the neuroblasts, while the remainder form an epithelium that lines the neural canal, thus giving origin to the astrocytes and the ependymal cells.

All of the nerve cells that compose the peripheral ganglia come from cells that have migrated from, or have separated themselves from the neural canal. In all of these cases the neuroblasts are escorted by indifferent cells, which accompany nerve cells everywhere and are to be found in all ganglia.

The peripheral nerves grow in the way already described from neuroblasts situated either centrally or peripherally. Up to a certain stage in its development a peripheral nerve consists wholly of neurofibrils and axoplasm; then the indifferent cells just mentioned accumulate along it and enclose it with a sheath of Schwann, which is therefore the primary sheath of the nerve. This may remain its only coat, or nerve medulla may develop in its cells and gradually enwrap the axis cylinder with a medullary mantle. In the central organ, where the sheath of Schwann is not found about the nerve fibers, the function of forming the medulla is taken over by the glia cells, which are, to a certain degree, the functional equivalents of the cells of Schwann.

The Supporting Tissues

The final class is the supporting tissue, which differs in many ways from the other three. This originates from the ***mesenchyma,*** i.e., from cells that leave the inner, middle and perhaps also the outer germinal layers and interpose themselves between the primary blastoderms. Only one supporting tissue develops directly from the entoderm, the chorda dorsalis, and this is of only transitory importance in man.

The tissues that have been heretofore described have active functions in the way of secretion, absorption, conduction, etc., but supporting tissue plays a *passive part*, giving, when fully developed, support and stability to the body. It not only forms the skeleton, but it is also a constituent of almost every organ in the human body, which it enwraps in special envelopes, separates one from another, and often enters and subdivides into smaller portions.

Supporting tissue also displays its passive character in that, at least in most cases, its essential part is situated not in the cells, but in an **intercellular substance** that is secreted by them and, if present at all in other tissues, is so to a very subordinate degree. This intercellular substance may or may not have a definite form; it may be soft and like mucus, firm and flexible, or hard and rigid, so it is best to differentiate this tissue in accordance with the nature of the intercellular substance present with it.

We may first divide supporting substances into two large groups, those with little or no intercellular substance, and those with such substance.

1. **Supporting tissue with little intercellular substance.** A supporting function can be exerted by such a tissue as this only by the cells themselves when they are placed close together and a certain power of resistance is imparted to them by the development of fluid within them, and the formation of a firm, membranous crusta or pellicle. This class includes the ***chordal tissue*** and the ***vesicular supporting tissue.***

2. **Supporting tissue with intercellular substance.** This large group, which embraces the great bulk of the supporting tissues, needs to be subdivided according to the nature and formation of the intercellular substance. These subdivisions are:

a. One in which the intercellular substance is soft, of mucous or fluid consistence, and may contain fibrils. This includes the ***gelatinous*** and the ***vitreous tissues.***

BOSTON MEDICAL
DEC 4 1915
LIBRARY

b. One in which the intercellular substance consists wholly of fibrils that are not intercellular for the most part, but remain enclosed in the cell bodies. The ***reticulated*** or ***adenoid supporting tissue*** belongs in this category, and we might add the ***neuroglia tissue*** which has already been described.

c. One in which the intercellular substance consists of fibrils that are free from the cells to a much greater extent. No other material is added in either this variety, or in any of the preceding. Here belongs the true ***connective tissue*** with its subgroups to be described later.

d. One in which the intercellular substance consists of fibrils which are consolidated by a secretion from the cells which is of firm consistence and hyaline appearance. This embraces ***cartilaginous tissue.***

e. One in which the intercellular substance consists of fibrils that are impregnated with lime salts and unite to form lamellæ which are joined together by a cement. This tissue possesses firmness and the power of resistance to an extraordinary degree, and furnishes in the ***osseous tissue*** the most perfect type of support.

The Chordal Tissue

The support of the embryonal human body in the early stages of its development is furnished by a cord situated between the neural and the visceral tubes in the axis of the body and known as the **chorda dorsalis,** or **notochord.** This will receive only a brief mention here as it is of quite subordinate importance in the adult body. Its tissue consists of **chordal cells,** which are vesicular, vary in size from medium to large, and have shapes that depend materially on the closeness with which they are packed together. A fluid is formed within the cells by a liquefaction of the protoplasm, and the turgor thus produced imparts a certain degree of firmness to the tissue. Externally a very dense ectoplasm encloses the cell as with a membrane, and may contain fibrillary formations, the so-called tonofibrils. The chordal cells are covered by a layer of small protoplasmic cells, the **chordal epithelium,** which is their matrix, and then follows the **chordal sheath** that envelops the entire chord. In proportion as the vertebral column approaches development the notochord disappears, so that at birth only some slight traces of its tissue remain in the so-called ***gelatinous nucleus of the intervertebral discs.***

The Vesicular Supporting Tissue

The principal characteristic of vesicular supporting tissue is the presence of large vesicular cells that contain fluid under sufficient pressure to keep them tense. Externally each cell is enclosed in a sort of membrane that resembles a crusta and, like it, is immediately connected with the protoplasm of the cell body. As a rule, the cells lie together in large masses with true connective tissue fibrils between them (Pl. 15, Fig. 44).

Although this tissue is of frequent occurrence in the lower animals, it is found in man in only a few such places as the little sesamoid bones in the tendon of the peroneus longus.

The Gelatinous Tissue

This forms in man and the higher mammals in the forerunner of fibrillary connective tissue, and is to be found in its pure form only in young embryos, as it early passes through transition stages into connective tissue by the development of fibrils. It is preserved longest in the ***Wharton jelly*** of the umbilical cord. Gelatinous tissue is composed of medium sized cells that are not aggregated very densely and are provided with numerous processes which anastomose and form a protoplasmic network having more or less large meshes. These meshes are filled with **jelly,** a secretory product of the cells, which therefore represents here the intercellular or basic substance of supporting tissue. This jelly is of semisolid consistence and is probably a mixture of true mucin, which is insoluble in water and can be precipitated by acetic acid, and mucoids, which are soluble in water and cannot be precipitated in that way.

The Vitreous Tissue

Although the greatly branched cell is an important constituent of the gelatinous tissue, the vitreous contains either none at all, or only a few unimportant ones in places. The place of the cellular network is taken by a maze of extremely delicate **fibrils** that branch, anastomose, and form meshes, some close, some wide, according to their location. These meshes contain a fluid known as the **vitreous humor,** which contains mucoids, but no mucin. Unlike the gelatinous tissue the vitreous is not exclusively of mesenchymatous origin, for cells from the ectoderm, particularly those of the inner layer of the retina and of the lens, take part in its formation. They send out very minute processes and form the matrix of the vitreous tissue, and later have added to them wandering cells from the mesenchyma.

The Reticular Tissue

Reticular shows an unmistakable likeness to gelatinous tissue, of which it is simply a development in that it is formed fundamentally of branched anastomosing cells, but there is no gelatinous basic substance filling the meshes of the network. The characteristic feature of this tissue is the differentiation of **fibrils** in the cells, which are not confined to the cell bodies, but extend into the processes and so form a second **fibrillary network** within the protoplasmic net. In time the fibrils become strong fibers with many branches, but they always maintain their intracellular position, though often they are quite superficial and are covered by only a very thin layer of protoplasm (Pl. 15, Fig. 43).

This is preeminently the form of the supporting tissue of the lymphatic organs. When lymph cells accumulate in its meshes it becomes **adenoid** or **lymphoid** tissue. It is found in the lymphatic glands, the tonsils, the follicles of the intestinal wall, the thymus, the spleen, and it also forms the tunica propria of the stomach and the intestines.

The Neuroglia Tissue

Though this has been dealt with under the description of nerve tissue it should be mentioned in this place. Like the vitreous it is of ectodermal origin, and consists of cells and intracellular fibers like the reticular tissue, but differs from the latter in that its cells do not form a network, and its cell processes run out freely. Neuroglia fibers also have a greater degree of independence than those of the reticular tissue, as they are in places intercellular in their courses.

The Connective Tissue

Connective tissue, also known as **fibrillary connective tissue,** is the most widespread of all the supporting substances in the human body. It comes from gelatinous tissue and is therefore of mesenchymatous origin. It is characterized by the development of an intercellular substance composed of fibers which casts the cells far into the background. We need to consider it minutely because of its importance, and will first study more closely its two components, its cells and its fibers.

Although the **cells** are greatly overshadowed by the fibrous intercellular substance, the part they play is very important and they show a great diversity in form and construction. They are all derivatives of those branched, mesenchymatous cells with which we became acquainted in gelatinous tissue, with the addition of numerous blood cells that, at a later period, wander out from the vessels and enter the gaps and chinks to be found everywhere between the connective tissue fibers. Mesenchymatous cells have a great capacity for transformation. They may produce fibrous intermediate substance and thus pose as **fibroblasts,** the true connective tissue cells, or they may undertake other functions and, without producing any intermediate substance, may sever their connections with their neighbors, draw in their processes, cause their bodies to assume a spherical form, and then, like certain colorless blood cells, make amœboid movements and become known as **wandering cells.** Still, all of the wandering cells of the connective tissue are not mesenchymatous, many of them are lymphocytes that have migrated from the blood vessels. The two varieties possess the same characteristics and cannot be distinguished apart later. It is also uncertain but what fibroblasts of the perfected connective tissue may in later life be transformed likewise into wandering cells. These wandering cells undergo many changes; they may become stationary again and form **clasmatocytes,** or they may become **plasma cells,** or **mast cells,** through special changes in their bodies. As these changes may all occur in a cell that has wandered into, or has originated at a place, we must look upon both the connective tissue cells and the colorless cells of the blood as ancestors of these various forms. We will now study rather more closely the individual kinds of cells met with in the fully developed connective tissue.

The characteristics of the mesenchymatous cells remain fairly well preserved in the **fibroblasts,** often called the **fixed connective tissue cells** (Pl. 12, Fig. 36, fbl), which are large and stellate, have numerous processes, and have shapes that depend materially on their locations. By means of their processes

they are closely attached to the fibers of connective tissue and often accompany them for considerable distances. The processes of neighboring cells frequently anastomose, but, as a rule, without forming a closed protoplasmic network. The arrangement of the cells, like their shapes, is dependent to a great degree on their location; they are to be found scattered about, grouped in irregular masses, and in regular formations.

An important attribute that fibroblasts have in common with many other kinds of cells is the power to appropriate fat. The fat of the human body is a variable mixture of free fatty acids, stearic, palmitic, and oleic, and neutral fats, i.e., the propenyl ethers of these acids. It is introduced into the organism with the food, broken up in the intestine, absorbed by the cells of the intestinal epithelium, recombined, and carried to all of the organs by way of the circulation of the blood and lymph. In the fibroblast it makes its first appearance in the form of very minute, strongly refractive particles that blend very soon into large drops, which may enlarge so much by accretion as to reduce the cell protoplasm into a narrow marginal zone about the nucleus. This we call a **fat cell** (Pl. 14, Fig. 42).

Under the microscope these drops of fat become evident through their great *refractive power;* each acts as a convex lens. Another characteristic is the deep black stain imparted to them by osmic acid in consequence of their *deoxidation power.* They may also be stained red by such dyes as sudan and scarlet.

Pigment is very often met with in the body of the fibroblast, where it appears in the form of little yellow, brown, or black granules that are embedded in the protoplasm and may be agglomerated into large masses. Fibroblasts that are thus pigmented are called **pigment cells** (Pl. 14, Fig. 41). They can be recognized from the facts that their bodies are much branched, and that they are highly capable of moving about so as to be able to carry the pigment from one place to another, as, for example, to the epithelium. Whether the pigment comes from the blood, or is elaborated in the cell bodies themselves, remains an open question. It is also uncertain whether the pigment cells, which play an important part in the lower animals under the name of chromatophores, are really mesenchymatous elements, or may not be wandering cells from the ectoderm.

The **wandering cells** are derived from the mesenchyma, as before stated, in that the bodies of the mesenchymatous cells become rounded and mobile. They multiply greatly and wander everywhere throughout the connective tissue. In later embryonal life this transformation of fibroblasts is greatly overshadowed by the immigration of large numbers of lymphocytes from the blood vessels, which also become wandering cells. Wandering cells vary a great deal in form and size, but are always smaller than the fibroblasts. This is also true of their nuclei, which are always very rich in chromatin and are often irregular in shape. The cell bodies exhibit no peculiarities aside from the changes in shape brought about by the amœboid movements. The wandering cells are to be met with in all parts of the connective tissue and elsewhere as well, for they frequently pass out of this tissue into the epithelium that covers it, and into the cavities of the body (Pl. 1, Fig. 3; Pl. 8, Fig. 26; Pl. 9, Fig. 27;

Pl. 11, Fig. 35). The most important attribute they possess is the capacity to surround and incorporate foreign substances through their power of amœboid movement. They thus dispose not only of dead constituents of the normal body, but also of elements that have penetrated from without, foreign bodies, bacteria, and the like. In doing this they play an extremely important part in the economy of the body by rendering harmful substances innocuous and have consequently received the name of **phagocytes.**

The **clasmatocytes** are similar in certain ways to the fibroblasts; they are of the same size and branch in a like manner (Pl. 12, Fig. 36, cl). The nuclei are always rather smaller, the cell bodies are basophilic and always contain very variable granules capable of being stained, scattered irregularly through them. Modern researches seem to show that clasmatocytes are nothing else than resting wandering cells.

Plasma cells are more rounded and are to be found but sparsely in the connective tissue. The nuclei are small and have near them distinct ***central bodies*** within a clear areola. The protoplasm is more strongly basophilic than that of the clasmatocytes. We must regard them as special modifications of wandering cells.

A very characteristic form of the connective tissue cells has been named by *Ehrlich* **mast cells,** and he believes that they are produced from fibroblasts by fattening (Pl. 12, Fig. 36, mz). They are roundish, or rather elongated cells *without processes,* which are very numerous in the subcutaneous connective tissue and are characterized by the presence of many ***large granules*** within their cell bodies. While these granules stain with basic dyes they do not take the color of the dye inself, but rather that of its free color base (Pl. 50, Figs. 119 and 121, mz). For example, thionin is the base of thionin hydrochlorate; the color of the dye is blue, that of its base is red, and when mast cells are stained with this dye the nuclei become blue while the granules become red. The granules of the mast cell share this attribute, which is called **metachromasia,** with many other constituents of tissue, for instance mucus. Mast cells are to be found only in the connective tissue, never in the blood. They multiply by mitosis and originate perhaps from the clasmatocytes.

A final constant constituent of connective tissue is found in the **eosinophile leucocytes,** which are also to be found normally in the circulating blood (Pl. 12, Fig. 36, eoz). They are of medium size and contain in their bodies many *fine granules* which usually surround the nucleus closely, are oxyphilic, and are stained with peculiar intensity by eosin. The form of the nucleus varies; it may be dumbbell-shaped, lobulated or annular. Whether all of these cells have migrated from the blood vessels, or whether some at least are derived from the wandering cells in the connective tissue, still remains an open question.

The **intercellular substance** of the connective tissue consists of fibers which arise in the superficial layers of the cells, but later become free and then show ability to grow independently. They are divided into two varieties, the ***collagenous*** and the ***elastic fibers,*** in accordance with their chemical, physical, and morphological characteristics.

The **collagenous fibers,** also called simply **connective tissue fibers,** generally resemble bands, but sometimes round cords, that vary in length and

thickness (Pl. 12, Fig. 36, colf). An indistinct longitudinal striation, that may often be noticed, is the imprint of the fact that they are composed of very minute ***fibrils*** bound together with a very small quantity of cement. The cement may be dissolved away by treating the fiber with lime water, or baryta water, so as to allow the rather swollen fibrils to become free. The fibers unite to form bundles of greater or less thickness, and the individual bundles may branch and join together to form networks, but this is not always the case.

As regards their ***physical and chemical properties*** the collagenous fibers are colorless, elastic, have only a slight luster, and are doubly refractive. They swell in aqueous dilutions of alkalies and acids, especially of acetic acid, into an almost homogeneous, glassy mass. In the first stage of this swelling bundles are to be seen that appear to be bulging in places, while between these bulges the swelling of the bundle is impeded by encircling cell processes. These fibers become completely dissolved in water heated in 120°C. and form a gelatinous mass on cooling. The dissolution takes pláce more easily if the fibers are first caused to swell by the addition of dilute acetic acid, and then heated. Chemically the fibers consist of **collegen,** and albuminoid that is changed by boiling into **glue,** or **gelatin,** to which they owe their name. Another important peculiarity of these fibers is that after they have been swollen by treatment with an acid they become dissolved by the gastric or the pancreatic juice with the formation of gelatose. As regards staining they are oxyphilic.

The **elastic fibers** vary much in caliber; sometimes they are immeasurably slender, but in many cases they have a considerable thickness (Pl. 12, Fig. 36, elf; Figs. 37 and 38). They possess quite a number of marked characteristics that enable us to differentiate them easily from the fibers just described. They can never be made out to be composed of fibrils. They incline strongly to branch and anastomose, and they may form ***networks*** so extensive as to look like ***fenestrated membranes*** through a broadening of the fibers with a corresponding diminution in the size of the meshes. As implied by their name they are much more elastic than the collagenous fibers. When cut across they retract with a characteristic rolling in of their free ends. Wherever they are collected in large numbers they present a yellowish white color that distinguishes them clearly. Elastic fibers have a much greater luster than the collagenous, in consequence of their higher power of refraction, but they are less strongly anisotropic. They also exhibit a much greater power of resistance to physical and chemical agents; they do not swell, but simply become dissolved in concentrated mineral acids, yield no gelatin on boiling, and are more resistant to the gastric and pancreatic juices. They consist of **elastin,** an albuminoid closely related to collagen, but containing less sulphur, which shows affinity to both acid and basic dyes. In microscopical preparations the elastic fibers, when present in small numbers, are not easy to distinguish from the mass of collagenous, but they can be brought out at once, when the tissue is fresh, by the addition of a drop of dilute acetic acid, as this causes the collagenous fibers to swell and leaves the elastic fibers sharply differentiated.

Mention should be made here of a peculiar kind of fibers found in only a few places in the human body, e.g., in the parenchyma of the liver, the **lattice fibers.** These are for the most part very delicate and tortuous, for exquisite

networks, and are to be distinguished from the elastic fibers through their chemical and staining reactions. Chemically they resemble collagenous fibers, into which they change in many places, but they must differ as they are much more unyielding and can be demonstrated only by the aid of the gold and silver impregnation method.

Now that we have learned to recognize the various elements of which connective tissue is composed, we will turn our attention to the various forms in which this tissue appears in the human body, which are, in accordance with the arrangement or character of the intercellular substance, and the peculiarities of the fibroblasts, ***loose connective tissue, tight connective tissue, elastic tissue, pigmented connective tissue,*** and ***fat tissue.***

1. **Loose connective tissue** is distributed very widely throughout the human body. It forms the supporting framework of each of the parenchymatous organs, frequently subdivides these into lobes and lobules, joins the skin to the musculature, separates the muscles, forms the sheaths of the muscular fasciculi, and joins many organs together. The characteristic feature of this tissue is that its bundles of fibers have no regular arrangement, but cross and interlace in all directions. Wide interspaces exist between the bundles, which are filled with lymph, afford abundant opportunity to the wandering cells for their movements, and are in open communication with the system of lymphatic vessels of the body.

2. **Tight connective tissue** originates from the preceding under the influence of such mechanical forces as tension and pressure, which force the bundles of fibers tightly together and into regular courses to form cords or plates. It is found in the tendons, fasciæ, aponeuroses, and ligaments, as well as in the sclera and cornea. The interspaces filled with lymph, that exist in loose connective tissue, are naturally done away with either entirely or for the most part, leaving only room between the bundles for the cells. The latter also lack the profusion of form that typifies those of loose connective tissue. They are chiefly fibroblasts arranged characteristically in columns or rows, one cell directly adjoining another. Thus in tendons the connective tissue fibers form bundles that run longitudinally with the cells lying between them in longitudinal rows. Each of these cells sends out winglike processes that penetrate between the tendinous bundles and surround them with an incomplete protoplasmic tunic. The fibroblasts, the so-called **tendon corpuscles,** thus come to present a stellate picture in cross sections of tendons, while in longitudinal sections cell bodies are to be seen irregularly following each other (Pl. 13). Loose connective tissue is moreover to be found associated with the tight in such organs as are composed of the latter.

When the amount of elastic fibers is considerably in excess of that of the connective tissue fibers we speak of an **elastic tissue.** This is usually met with in the form of coherent membranes, networks, or felted fibers, as in the walls of the blood vessels, and in the respiratory organs, but it may also be found in larger masses, as in the ligamentum nuchæ, which is only rudimentary in man. When fully developed it is composed of thick elastic fibers which run parallel to one another, are sheathed with cells in the same way as tendon fibers, and are separated from one another by collagenous connective tissue (Pl. 12,

Fig. 38). It can readily be distinguished macroscopically from either loose or tight connective tissue by its pronounced luster and its somewhat yellowish color, which has caused it to be called sometimes **yellow connective tissue.**

Pigmented connective tissue, or **pigment tissue,** is found in the human body only in the middle coat of the eye and in the iris. It is characterized by the fact that the fibroblasts have taken up pigment and become pigment cells, while between them lie networks of connective tissue and elastic fibers (Pl. 87, Fig. 188, chp).

Fat tissue occurs in the form of little lobules joined together into larger masses by loose connective tissue (Pl. 93, Fig. 197, sbc). Each lobule is composed of fat cells, i.e., of fibroblasts the bodies of which have become distended with fat. Connective tissue fibers appear, though very sparsely, between the individual fat cells. In well nourished, strong persons this tissue attains a high degree of development in the ***panniculus adiposus*** of the skin. It likewise forms a ***fatty capsule*** in the subperitoneal tissue about the kidney, and appears in great masses in the ***mesentery*** and ***omentum.*** When fat tissue is caused to retrograde by a suitable diet the nature of the change depends on the age of the individual; in young persons the fat cells change back into ordinary fibroblasts while their fatty contents atrophy, and the transformation is thus made into loose connective tissue, but in old persons the cells atrophy and a mucous fluid accumulates in them.

Cartilaginous Tissue

The intercellular substance of cartilage consists of the two constituents which form that of connective tissue, collagenous and elastic fibers, with the addition of an amorphous **basic substance** outside of these fibers, that is excreted by the cells and may cover up completely all of the formed constituents. This it is that stamps cartilage with its own physical properties and gives it a certain firmness combined with flexibility which renders it a true supporting substance. In order that we may understand the condition better it seems advisable that we review briefly the development of cartilage.

Cartilaginous tissue comes from the same mesenchymatous cells as connective tissue. At the places where it begins to appear these cells first lose their characteristic stellate form and become little roundish cells, lying close together, which are known as **chondroblasts.** Each of these embryonic cells gives off collagenous fibrils, but at the same time changes the peripheral layers of its body into a crusta, or sort of membrane, which remains throughout in continuous connection with the cell body, has the same staining reaction, and is therefore oxyphilic. The cells are thus moved somewhat apart from one another, and the cartilage enters upon the **prochondral stage.** We have here conditions similar to those presented by the vesicular supporting tissue, which may therefore be considered as intermediate between connective and cartilaginous tissues. Then comes the characteristic excretion from the bodies of the cartilage cells of a fluid containing **chondroitin-sulphuric acid,** which gives this substance the marked basophilic property that causes it to contrast with cell protoplasm. This substance naturally first permeates the crusta of the cell so

that it may be differentiated sharply from the cell body by staining. At the same time the crusta and the body separate morphologically, and a pellicle or cell capsule comes from the former. With this the cartilage enters its **protochondral stage.** The further development can be readily understood; a secretion comes unceasingly from the cells, appears between them as a basic substance and so surrounds and envelops the collagenous fibrils that they escape ordinary observation. The oxyphilic collagenous fibrils spread farther apart, and the protochondral passes into the **chondral stage.**

We have therefore to differentiate in fully developed cartilaginous tissue the **cartilage cells** and the **basic substance,** the latter of which envelops the **fibrils.** Ordinarily these fibrils cannot be detected readily in the basic substance, which alone is to be seen and gives the tissue the uniform, hyaline appearance of ***hyaline cartilage,*** but they may be more or less prominent, and then we speak of a ***fibrocartilage.*** In both varieties the fibrils are collagenous. When elastic fibers appear in the basic substance they exhibit a vary marked tendency to the formation of networks, and we have ***elastic cartilage,*** or ***reticular cartilage***

Hyaline Cartilage

Hyaline cartilage is found in man chiefly during a temporary stage in the development of the body framework, in which it exists alone for a considerable period during embryonal life as the **primordial skeleton.** Although it attains a firmness that is not to be underestimated, it is unequal to bear the burden of a human body, and is replaced by the far stronger osseous tissue during the second half of fetal life, or in part after birth. The lower we descend among the vertebrates the greater is the part we find this cartilage to play in the final skeleton, and in the lowest, the cyclostomata, the selachii, and many ganodei, it does not go on to the development of bone anywhere. In human adults hyaline cartilage is to be found chiefly as a covering to the ends of bones that come together to form joints, symphyses, or synchondroses, in places where tendons run in bony grooves, or some similar condition exists. It also forms the framework of the nose, larynx, trachea, and bronchi, but it should be noted that ossification takes place later in life in many of these places.

As regards the *physical aspect* of hyaline cartilage, it has a peculiar, unique consistence, is firm, elastic, flexible, easily cut, is bluish white in color, and is feebly lustrous. In thin layers it is translucent and doubly refractive. This latter property depends on the content of collagenous fibrils in its basic substance.

The **cartilage cells** lie in cavities, called **cartilage cavities,** two or more often together (Pl. 16, Figs. 45 and 46). The cells are of medium size, rich in protoplasm, and vary a great deal in shape on account of the limited quarters furnished by the cartilage cavities, in which they lie pressed together so closely as to flatten each other. They fill the cavities completely, and yet are quite sensitive to mechanical and chemical influences, which cause them to shrink back from their capsules and to shrivel. The same result can be produced by passing an electric current through living cartilage, the cells retract and do not return to their former shape.

The **cell body** is usually vacuolized (Pl. 16, Fig. 46). Many plasmosomes, some smaller, some larger, lie in the walls of the vacuoles, with near them thread-like rows of granules, the mitochondria. The contents of the vacuoles consists chiefly of **glycogen,** which is quite a characteristic constituent of cartilage cells. It appears in them in the form of large or small granules during fetal life, even after the basic substance has been formed, and is demonstrable in them until old age. The cartilage cell also contains minute particles of **fat,** that may blend into large drops, which appear before the glycogen and gradually disappear at the age of puberty.

Each cartilage cell contains a moderately large **nucleus,** which is usually spherical, though it may be ellipsoidal in the peripheral parts where the cells are larger (Pl. 16, Fig. 45). In young, growing cartilage the nuclei may often be seen in mitosis, and cells with two nuclei are frequently to be observed. In the latter cases the segmentation of the cell body did not follow that of the nucleus immediately (Pl. 16, Fig. 46, b).

The **basic substance** of hyaline cartilage appears in the fresh section to be uniform, dull, and without structure, except that immediately about the cells are to be found the **cartilage capsules,** which become evident as narrow edges through their somewhat stronger refractive power. More of its structure is revealed when the cartilage is fixed in a suitable manner. Then it can be seen that the entire basic substance is divided into two portions, the **cell territories,** and the **framework.** The cell territories are islands of basic substance that enclose two or more cartilage cells with their capsules, and are separated from one another by a net or framework composed of the rest of the basic substance. Still more details may be brought out within the cell territories if we stain with a suitably chosen mixture of an acid and a basic dye (Pl. 17, Fig. 47). Each cartilage cell is enclosed in a strongly **basophilic cartilage capsule,** those of neighboring cells frequently blending. About the cartilage capsule, enclosing two or more encapsulated cells, lies a rather broader ring which is much less ***basophilic;*** this we call the **inner cell areola.** Several inner cell areolæ are finally embraced by an **outer cell areola,** which is not basophilic, but ***oxyphilic.*** The outer cell areola together with its contents constitutes a **cell territory.** The **framework** may be distinguished from the outer cell areola by the fact that it is much less ***oxyphilic,*** or is perhaps very feebly basophilic.

The entire basic substance of hyaline cartilage is permeated by **collagenous fibrils.** These can scarcely be seen in fresh tissue, and only under very favorable circumstances, as in the superficial layers of a joint cartilage. If we first treat the tissue with gastric or pancreatic juice they can be seen very well with the polariscopic microscope. They run in parallel courses about the cartilage cells and form a dense felt of minute fibers in the framework. The differences of stain mentioned above to be seen in different parts of the basic substance depend on the preponderance in any place of the oxyphilic collagenous fibrils, or of the basophilic basic substance. When the former predominates, as in the outer cell areola, the tissue appears to be oxyphilic, while if the latter has the ascendancy the collagen is obscured and basophilia prevails, as in the capsule and the inner cell areola.

Next to collagen the most important constituent of the cartilaginous basic substance is **chondroitin-sulphuric acid,** a monobasic nitrogenous acid, which is combined with an albuminoid and gives the substance its basophilic reaction. It is secreted by the cartilage cells, a fact that explains why the parts of the basic substance lying nearest to the cells exhibits the strongest basophilia. When cartilage is boiled the collagen contained in it yields a gelatinous substance known as **chondrin,** which differs from gelatin in its content of the compound of chondroitic acid with albuminoid, and of the mineral salts of the same acid.

A deposit of **lime salts** almost always takes place in old age in the basic substance of cartilage, which renders the elastic, flexible tissue rigid and brittle. These salts appear first about the cartilage cells in the form of very minute particles, which soon unite to form large, calcareous masses. Cartilage can also *ossify* in later life, i.e., its tissue may be destroyed and replaced by that of bone. Calcification and ossification of cartilage are therefore two fundamentally different processes.

Its tissue changes at the periphery of the cartilage, its basic substance constantly decreasing and its cells drawing closer together, and passes over into a compact, firmly built connective tissue permeated with elastic fibers, the **perichondrium,** which separates it from the surrounding loose connective tissue (Pl. 16, Fig. 45). The perichondrium is rich in cells, and its fibroblasts may become cartilage cells by cutting themselves off with basic substance. Hence the **appositional growth** of cartilage comes from the perichondrium. Growth also takes place within the substance of cartilage itself by segmentation of the cartilage cells and the secretion of basic substance; this is called its **interstitial growth.**

Fibrocartilage

By **fibrocartilage, or connective tissue cartilage,** we mean a cartilage in which the collagenous fibers can be distinctly seen without special preparation. Such cartilages are not too abundant in the human body. They are to be found chiefly in the intermediate discs and the margins of the sockets of the various joints, the fibrocartilagines intercalares, and the labia glencidalia. Examples are the articular cartilages of the sternoclavicular and knee joints, the outer, laminar parts of the intervertebral discs, and the interpubic fibrocartilages.

The picture presented by fibrocartilage under the microscope is extremely variable, because of the transition forms that may be exhibited, on the one hand into tight connective tissue, on the other into hyaline cartilage. In the former case lines of cartilage cells are to be found between the densely packed, parallel collagenous fibers, each provided with a distinct cartilage capsule, while scarcely anything more is to be seen of the basic substance. The appearance of the hyaline basic substance becomes more distinct as the cartilage cells become more pronounced; it may be seen as cartilaginous islands or bands within the tight connective tissue, and finally preponderates in bulk to such an extent that the collagenous fibers are completely hidden and the typical picture of

hyaline cartilage is developed (Pl. 17, Fig. 48). Elastic fibers are to be found here and there among the collagenous, but they are in no way prominent. When the basic substance of cartilage is not present, or simply forms the cartilage capsules, this tissue has been called **chondroid connective tissue.**

Elastic Cartilage

Collagenous fibers are strongly in evidence in fibrocartilage, but in **elastic,** or **reticulated cartilage** the structural picture is dominated by networks of **elastic fibers.** Like fibrocartilage this variety is found in only a few places in the human body. It forms the framework of the auricle, external auditory canal, and Eustachian tube, and takes part in the structure of the larynx, where it forms the epiglottic, santorinian, and part of the arytenoid cartilages, particularly of the vocal processes of the latter.

The cells of elastic cartilage differ in no way from those of hyaline, and its basic substance is of the same composition, but **elastic fibers** are added, which can be readily seen without staining, impart a rather yellow color to the cartilage, make it less translucent, and increase its power of resistance. They are sometimes extremely delicate, sometimes coarser, and may attain quite a considerable thickness (Pl. 16, Fig. 49). They give off many branches which anastomose and form networks that permeate the entire basic substance of the cartilage and hold the cartilage cells in their larger meshes. At the periphery of the cartilage these networks pass over without interruption into the elastic fibers of the perichondrium. The peripheral fibers are the thinnest and run for the most part parallel to the surface of the cartilage, but farther in they become thicker and placed more vertically to the surface, while in the center they again become thin and form at this place an extremely dense, fine-meshed felt.

Osseous Tissue

The supporting substance of the human body attains its highest development and its greatest functional capacity in bone, a tissue that appears very late in the course of evolution. No bone is developed in the invertebrates, or in the lowest vertebrates, the amphioxus and the cyclostoma. Ossification appears first in the connective tissue of the skin of the selachians, where it forms a protective **exoskeleton,** which reaches its highest development among the reptiles, in turtles and crocodiles. Later, bony tissue develops in the cartilaginous, as in the skin, for the purpose of forming an **osseous endoskeleton,** which first appears in the ganoids and is wholly absent in the selachians. Bone may therefore originate directly from connective tissue, or in connection with cartilage.

We meet with something similar in man. The great majority of his bones, those of the vertebræ, the limbs, the base of the skull, and of the tongue, are cartilaginous at first and are called **primary,** while those of the sides and vault of the skull, and those of the face originate directly from connective tissue and are said to be **secondary bones.**

The formation of bony tissue proceeds from cells called **osteoblasts.** Opinions are still divided with regard to the origin of these cells; the majority

of histologists consider them to be fibroblasts, i.e., connective tissue cells, but some think them to be cells that have migrated from the ectoderm. In the simplest formation of bone these stellate cells are deposited thickly upon the bundles of collagenous fibers and are bound there by a cement containing lime, causing the collagenous fibers to calcify. The cells then secrete more fibrils and cement about themselves and thus come to lie in a substance composed of collagenous fibrils enveloped in a material containing lime, the **basic substance of bone.** Now a second layer of osteoblasts begins, through the activity of which another layer of basic substance is formed, and so on. The result of this is that the completed bone tissue has an exquisite lamellated structure. Between the lamellæ of basic substance lie the bone cells, the former osteoblasts.

This is the simple course of ossification in the secondary bones, those that originate directly from the connective tissue, but the conditions are much more complicated in the primary bones. In these bones is deposited layer on layer in a quite similar manner on the surface of the cartilage from the richly cellular perichondrium, forming the **perichondral ossification,** but osteoblasts also penetrate with the blood vessels into the interior of the cartilage, where they destroy the tissue and hollow it out to form the **primary medullary cavity,** from which ossification proceeds to transform what remains of the cartilaginous tissue, **endochondral ossification.**

We need to study this last process rather more closely. At one or more points, called **ossification,** or **calcification points,** lime salts are excreted by the cartilage cells into the surrounding basic substance. Toward these points the richly cellular perichondrium proliferates, and there the cartilage is destroyed, the cartilage cells die, and a hollow cavity, filled with a very cellular periosteal tissue and blood vessels, is formed at the site of the calcification point, the **primary medullary cavity.** As this cavity enlarges with the advancing destruction of the cartilage, trabeculæ are preserved and remain joined to the principal mass, the **directing trabeculæ of the ossification.** Upon these the osteoblasts lodge and begin their bone forming activity, so that each bony trabecula that originates from the directing trabeculæ contains within itself at first a cartilaginous one, which later ossifies. This formation of bone with coincident destruction of cartilage extends gradually from the medullary cavity toward the periphery, until finally the endochondral and perichondral ossifications meet. Endochondral ossification is productive of a network of anastomosing bony trabeculæ, which form **spongy bone substance,** while the periosteal ossification gives us **compact bone substance.** The *blood vessels* play an important part; on the one hand, they destroy cartilage in their advance from the medullary space; on the other, they become grown about by newly formed bone in the perichondral ossification, and so come to lie in bony grooves that later become tubes, together with the osteoblasts that accompany them. Thus it happens that compact bone substance is traversed by a system of tubes, the **Haversian canals,** which lodge the nutrient blood vessels. The final form of the medullary cavity is determined later by the partial destruction of the remodeled bone substance by certain large, polynucleated cells, the **osteoclasts,** the genesis of which has not yet been learned with certainty. Some believe them to be metamorphosed fibro-

blasts, others think that they come from the epithelium of the blood vessels, and still others hold them to be cartilage cells that have been set free by the destruction of the cartilage.

Following this review of the development of bone tissue, we have to inquire more minutely into its construction, and to become somewhat acquainted with its *physical properties.* As stated above, it exceeds cartilage in firmness and hardness, and it cannot be cut, when fully developed, because of the lime salts it contains, but when the latter have been removed by treatment with dilute mineral acids we find it to resemble cartilage. On the other hand, if the organic substance is destroyed by heat, it becomes very brittle and friable. Thin layers of bone tissue are quite translucent and have a high degree of anisotropia due to the quantity of collagenous fibrils that they contain.

Wherever bone tissue is present in considerable quantity its **basic substance** has a markedly **lamellar** structure, due to the deposit of osteoblasts in layers on the collagenous fibrils in its development (Pl. 20, Fig. 52). Each lamella is composed of ***collagenous fibrils,*** bound together with ***cement.*** If a thin section of bone is carefully heated red hot so as to destroy the former, the cement alone will be left, and may be seen to be permeated by a great many densely packed tubes, which are the spaces in which the fibrils lay. The fibrils are grouped into little bundles in the lamellæ, those in each lamella running about parallel, but those in different lamellæ running in various directions, so that the fibrils in one may be perpendicular to those in another, and in a cross section through several lamellæ we may see in one points formed by the transversely cut fibrils, and in another, often adjoining, lines where they have been cut longitudinally. Punctate and striate lamellæ may alternate. If we examine such bone lamellæ with the polariscopic microscope we will find that in a certain position of the analyzer the striate lamellæ appear to be dark, the punctate light, and that when the ocular has been rotated 90° both appear to be of the same brightness. This is known as **pleochroism.**

In addition to the fibrils that form a constituent of the lamellæ, we find in the superficial layers of bone tissue bundles of thicker collagenous fibrils, which are often very thick, intermixed with elastic fibers. These do not belong to the individual lamellæ, but pass through them vertically or obliquely from the periosteum. They are known as **Sharpey's fibers,** and appear much more in embryonal than in fully developed bones.

The **cement** unites the collagenous fibrils into bundles, fills the spaces between the latter in the lamella, and finally binds the lamellæ together. It holds the ***lime salts.***

In speaking of the *arrangement of the lamellæ of the basic substance,* it should first be understood that when bone tissue exists simply as an extremely thin plate, no lamellæ are formed, and that the fibrils run only in one direction. As soon as the plate becomes somewhat thicker lamellæ appear with their surfaces parallel, but the arrangement becomes much more complicated wherever the mass of tissue is considerable, as in the ***compact bone*** found in the diaphyses of the long, and the cortices of the flat, bones.

In a cross section through the diaphysis of a human humerus we can distinguish three different systems of lamellæ (Pl. 18, Fig. 50). First we

have lamellæ that run parallel to the outer and inner surfaces of the bone; these are the **basic lamellæ,** which we may subdivide into the outer and the inner. They form only a comparatively small part of the entire bone, and are far surpassed in bulk by another system situated between them, which we call the **special** or **Haversian lamellæ.** These give the bone its peculiar structural imprint, and appear in the section as more or less regular concentric circles about a hole. Substantially each Haversian system of lamellæ consists of a hollow cylinder with very thick walls, which are in turn composed of several cylinders of basic substance, one within another. The hollow cylinder encloses the **Haversian canal,** which frequently does not lie exactly in its axis. In a longitudinal section of bone (Pl. 19, Fig. 51) the Haversian canals may be seen to run nearly parallel to one another, to unite by means of oblique branches, and so to form a system of canals throughout the bone substance for the accommodation of the nutrient vessels.

Each system of Haversian lamellæ consists of an indefinite number of single lamellæ; the systems lie at various distances apart, and are sharply differentiated from the surrounding bone tissue. This latter, which occupies the entire space between the systems of Haversian lamellæ and the outer and inner basic lamellæ, presents what are called the **interstitial** or **interposed lamellæ,** some of which run parallel to the outer basic lamellæ, while the rest follow no typical course.

The systems of Haversian lamellæ are united with the interstitial lamellæ that surround them by a cement that gives rise to the outlines which sharply delimit the systems in the cross section, the **cement lines** (Pl. 20, Fig. 52). The cement lines are always irregular, with many bulges jutting outward, and not only form frames to the Haversian lamellæ, but also divide the interstitial into separate systems.

The **basic substance of bone** differs in its *chemical composition* from every other tissue of the human body in the great amount of its mineral constituents, which comprise from 30 to 40% of its mass. The chief of these is calcium phosphate, followed at a long distance by calcium carbonate, magnesium phosphate, calcium fluoride, calcium chloride, and ferrum oxide. Of the organic constituents, which amount to 20 to 25%, the most important is **ossein,** a collagen mixed with mucoid and albumoid.

The **bone cells** represent the original osteoblasts, and lie in little cavities of the basic substance, the **bone cavities** or **lacunæ** (Pl. 21, Figs. 53 and 54). These lacunæ are shaped like pumpkin seeds, and are always intralamellar, a row of them to be found between every two lamellæ. In each row they lie apart at a certain distance and send out numerous branching tubules in all directions, the **bone canaliculi,** which run through the lamellæ and anastomose not only with neighboring canaliculi, but often with others situated at a distance, and thus form a system of canals that permeates the entire basic substance and permits the circulation of the nutrient fluid. The canaliculi of the innermost row of lacunæ in each Haversian system open directly into the Haversian canal.

Each lacuna and each canaliculus is surrounded by a thin layer of basic substance, called the **limiting sheath,** which may be isolated by treating

thin discs of bone for several hours with concentrated hydrochloric acid. Bodies shaped like pumpkin seeds and provided with many processes may then be seen, the so-called **bone corpuscles,** which conceal within themselves the bone cells. These limiting sheaths are composed of a specially modified, resistant layer of basic substance that contains no collagenous fibrils (Pl. 21, Fig. 55).

In the lacunæ lie flat cells provided with many processes that extend into the canaliculi. These are the bone cells. How far their processes go, and whether they anastomose with those of the neighboring cells, are questions that are not easily answered (Pl. 21, Fig. 56).

Dentine is a variety of bone tissue which will be described in the discussion of the structure of the teeth.

C

MICROSCOPIC ANATOMY OF ORGANS

I. THE VASCULAR SYSTEM

1. THE BLOOD

The blood, which carries nutriment and oxygen to all parts of the human body, consists of a fluid known as the **blood plasma,** and of corpuscular elements suspended in it, the **blood corpuscles.** We have to deal here chiefly with the latter, which are very closely related to the cellular elements of the connective tissue, as must be evident from what has been said in the preceding chapter and is particularly prominent in the part on embryology, as both come from the mesoderm.

The first signs of the formation of the blood are met with in the wall of the vitelline sac in the form of the so-called **blood islands.** These are masses of cells that have wandered out from the mesoderm, and have spread out between it and the vitellus like a network. The peripheral cells unite very soon, to form a continuous epithelium, while those situated more internally remain isolated and float about in a fluid secreted within the blood islands. The epithelial tube separates its contents from the neighboring mesoderm and vitellus, and forms the most primitive part of the blood vessel that thus originates. The cells that remain isolated are the **primitive blood corpuscles,** or the **primitive mesamœboids.**

While the formation of blood vessels proceeds subsequently in like manner in the embryonal body, important changes take place in these primitive mesamœboids. First they multiply by indirect segmentation many times repeated, then a not inconsiderable portion of them wander out of the primitive vessels into the surrounding mesoderm, and above all they exhibit an advancing differentiation in two principal directions. Part of them elaborate a coloring matter that contains iron, the **hæmoglobin,** envelop themselves with a membrane and become the red blood corpuscles, or **erythrocytes.** In doing this the corpuscles pass through various stages of transformation, manifest at first by a diminution in size and a greater staining power of the nucleus. The primitive mesamœboid enters the **ichthyoid** stage as a spherical cell containing hæmoglobin and a small nucleus, and in this stage it undergoes a lively multiplication by indirect segmentation. By the further diminution in size of the nucleus and massing of its chromatin, and by the enveloping of the cell in a membrane, it enters the **sauroid** stage, in which multiplication no longer takes place. The red blood cell then attains its final form by casting forth its nucleus, that has become pycnotic, and by flattening its body, so that finally, instead of a spherical, nucleated cell, we have a non-nucleated, flat, round disc, the young erythrocyte.

A certain percentage of the primitive mesamœboids that do not elaborate hæmoglobin within their bodies continue as they are for a long time, and are transformed into erythrocytes later in embryonal life, but the rest remain throughout life destitute of hæmoglobin and containing nuclei. These form the **white blood corpuscles,** or **leucocytes,** which are to be found in the blood of the adult bearing a certain percentage to the red blood corpuscles. While all of the erythrocytes present the same morphological picture in adults, the white blood corpuscles exhibit quite a variety of forms, but these are only developments, and finally degenerations of the young form.

The manufacture of blood in the embryo takes place not only in the blood vessels of the vitelline sac and of the embryonal body, but also at special chosen places, which are chiefly the liver and the bone marrow for the red blood corpuscles, the lymphoid organs, such as the lymphatic glands, the tonsils, the lymphatic follicles, and the spleen, for the white cells.

The Red Blood Corpuscles

The **red blood corpuscles,** or **erythrocytes,** form by far the greatest part of the corpuscular elements of the blood. A cubic millimeter of human blood contains between four and five millions of erythrocytes, and the ratio of their number to that of the leucocytes is about 500: 1.

The erythrocytes are round discs that have a diameter of 7 to 7.5 μ. They are considerably larger in the embryo, and under abnormal conditions such large erythrocytes may be found in the blood of adults, when they are called megalocytes. The thickness of an erythrocyte is greatest at its margin, where it is about 2 μ, and least at its center, so that it resembles a biconcave lens with a rounded margin.

When spread in a layer that is not too thin the erythrocytes, in consequence of a sort of capillary attraction, place themselves with their broad sides toward each other, like the separate pieces of a roll of coins standing more or less perfectly on their edges (Pl. 32, Fig. 80).

The color of the erythrocyte is a light yellow, depending on its content of the coloring matters of the blood, hæmoglobin and oxyhæmoglobin, the former of which is being produced constantly by reduction of the latter. Both are proteids easily soluble in water, insoluble in alcohol characterized by the iron they contain, and may be obtained in crystalline form very easily from many animals, but only with difficulty from man, **blood,** or **hæmoglobin crystals.** Hæmoglobin and oxyhæmoglobin have quite characteristic absorption spectra, and are found exclusively in the erythrocytes in firm combination with their substance. If distilled water is added to blood it becomes stained because it dissolves the coloring matter out of the corpuscles, while the blood becomes lake colored. The corpuscles themselves undergo an extensive change; they become less plainly visible and shadowy, on account of the loss of their coloring matter, and become much swollen. Dilute salt solution acts in a manner similar to distilled water on the erythrocytes, which are hypoisotonic to the blood serum. Stronger solutions of salt, which are hyperisotonic,

cause the erythrocytes to shrivel, to become indented, and to take the form of thorn apples or of morgensterns.

The erythrocytes are markedly oxyphilic; they stain with acid dyes, and owe this property to the coloring matters of the blood.

Very little is positively known concerning the minute structure of the erythrocytes. The fact that a nucleus is never present in adults has already been mentioned. Even with the greatest enlargement no structural details can be perceived in its body, yet for various reasons we have to suppose that it is enveloped in a membrane, which encloses a framework, or **stroma,** containing the blood coloring matters.

The White Blood Corpuscles

The **white blood corpuscles,** or **leucocytes,** differ in various ways from the erythrocytes, but chiefly in the absence of hæmoglobin and the presence of a nucleus. They are much fewer in number in the blood, but definite figures can hardly be given as their number fluctuates considerably, according to the place in the body, the age, and the physiological condition of the individual. The younger a person is the greater is the number of his leucocytes. A cubic millimeter of the blood of a new born child contains from 12,000 to 13,000. Blood taken from peripheral vascular areas contains more than that from central areas, and more leucocytes are to be found in the blood after a full meal than during hunger. The minimum number may be said to be 5,000, the maximum 10,000, the average 7,500 to the cubic millimeter of blood.

The leucocytes can always be recognized easily in the circulating blood from the fact that they roll singly along the wall of the blood vessel, while the erythrocytes occupy the axis of the vessel in a continuous current. Frequently the leucocytes remain hanging on the wall of the vessel, which indicates that these bodies have a certain stickiness. The erythrocytes are extremely plastic, as is shown by the fact that they very often are caused to undergo in the vessels many changes of form by the blood current that revert immediately, but this is not the case with the leucocytes, which are more resistant to such mechanical influences. On the other hand, they have, to a high degree, the power to change their own shapes, and to migrate from the vessels into the connective tissue, where we have learned to know them as wandering cells.

Leucocytes in a state of rest are more or less spherical cells, more rarely ovoid, that vary extremely in size. The smallest are about as large as erythrocytes, the largest attain a diameter as great as 20 μ (Pl. 31, Fig. 80).

The leucocytes of the human blood show essential differences in size, in the shape of the nucleus, and above all in the structure of the cell body. The latter may elaborate within itself fine or coarse **granules,** or **granulations,** which give the leucocytes a very characteristic appearance. The granulations are characterized by their form and their color reaction, and play a very important part in the classification of leucocytes. Various views are held as to their nature; some authors consider them to be secretory products of the cell body, others take them to be foreign bodies that have been seized by the

phagocytic leucocyte and are being worked up in its body, and still others believe them to be constant cell organs comparable to the microsomes of other cells, which take an important part in assimilation.

The following varieties of leucocytes may be differentiated in normal human blood:

1. **Lymphocytes.** These are spherical cells about as large as erythrocytes, 7 to 9 μ, with spherical or slightly indented nuclei that occupy the greater part of the cells and are surrounded only by a more or less narrow ledge of protoplasm. The nucleus exhibits a distinct framework, presents one or two nucleoli, and has a strong basic affinity. The same affinity is possessed by the cell body, in which distinct chondriosomes have recently been demonstrated. The body of the lymphocytes contains no true granulations (Pl. 32, Fig. 81).

Lymphocytes appear in the blood of children that are quite large and attain a diameter of even 15 μ, but differ in no way as regards their structure from those of adults. These are called ***lymphoblasts.***

Lymphocytes have amœboid properties and are able to pass through the walls of the vessels into the tissues, but this property is possessed to a considerably higher degree by the granular leucocytes.

A cubic millimeter of blood contains in children 7000 to 8000 lymphocytes. After the age of ten years the number decreases considerably, so that in the adult it is only 1500 to 2000. Hence in childhood the lymphocytes amount to from 40 to 60%, and in adults to only 20 to 25% of the total number of leucocytes.

2. **Transition forms.** These, which have a diameter of from 12 to 20 μ, are the largest cells of the human blood. The nucleus may vary a great deal in shape; it may be roundish, oval, have a slight indentation, or have greater indentations that give it a lobulated appearance, or it may be shaped like a horseshoe. The chromatin takes only a weak stain, so the nucleus appears light. In the cell body are to be seen delicate, but distinct granulations, that are neutrophilic, concerning the nature of which there is still a lively discussion (Pl. 32, Fig. 81).

The transition forms amount to only 6 or 8% of the total number of leucocytes.

3. **Neutrophilic leucocytes** form the great bulk of the colorless blood cells. They are of medium size, having a diameter of from 9 to 12 μ. The nucleus exhibits the most extensive polymorphism; usually it is broken into several little pieces that are joined together by slender bridges, which are frequently arched. These bridges often are so extremely delicate as to easily escape observation, and then the cells may seem to be polynucleated. The nucleus is rich in chromatin and stains strongly with basic colors. The protoplasm of the cell body is oxyphilic and contains many fine neutrophilic granules (Pl. 32, Figs. 81 and 82).

Four to five thousand are to be found in a cubic millimeter of blood, and they form 65 to 70% of all of the white blood corpuscles.

4. **Eosinophilic leucocytes.** These are somewhat larger than the neutrophiles, as they have a diameter of 12 to 15 μ. The nucleus is similar to that of the preceding, but on the whole is rather coarser, and its chromatin is more

weakly basophilic. But their distinguishing characteristic is furnished by the eosinophilic granules, which are coarse and regularly round in comparison with the granules of the neutrophiles. They refract light powerfully, have a peculiar yellowish color, and are strongly oxyphilic. They contain an albuminoid with much iron, which is in no way identical with hæmoglobin. In addition to this albuminoid, the eosinophilic granule contains a lipoid, a fatlike body, that gives it its great luster (Pl. 32, Fig. 81).

The blood of adults contains 100 to 200 eosinophilic leucocytes to the cubic millimeter; they therefore constitute only 2 or 3% of the entire quantity of white blood cells.

5. **Mast cells.** These cells, with which we became acquainted in the study of connective tissue, have a diameter of 8 to 10 μ. The nucleus has numerous indentations, is lobulated, is weakly basophilic, and appears very bright. Granules are embedded in the oxyphilic protoplasm, which are as large as, or larger than those of the eosinophilic leucocytes. They refract light weakly and are very soluble in water. In contrast to the eosinophilic granules they are decidedly basophilic and exhibit the phenomenon of metachromasia that has been described. They always contain glycogen, and may hold lipoids, like the eosinophilic granules.

Although the mast cells of the blood and of the connective tissue are very similar, there are weighty reasons which lead us to believe that the two have nothing to do with each other (Pl. 12, Fig. 36).

The mast cells form only a minute constituent of the normal blood; only about forty are to be found in a cubic millimeter, so they comprise not over 0.5% of the entire number of leucocytes.

Two theories exist today concerning the genetic relations of these varieties of leucocytes, one called the **polyphyletic,** the other the **monophyletic.** According to the former all granular leucocytes are well differentiated forms of cells that develop from one or more mother cells, or **myeloblasts,** situated in the bone marrow, while the blood cells that are not granular, the lymphocytes, differentiate themselves from the ***lymphoblasts*** formed in the lymphatic glands. This gives us two different primitive forms for all leucocytes, the myeloblasts and the lymphoblasts, coming from different places of origin.

According to the monophyletic theory there is, on the contrary, only one primitive form from which all leucocytes become differentiated. Once the cell has started in a certain direction it may multiply by segmentation, but it cannot be transformed into another kind of cell.

The Blood Platelets

Human blood contains, in addition to the erythrocytes and leucocytes, a third morphological element, the **blood platelet.** These are considerably more numerous in the blood than the leucocytes, as a cubic millimeter contains about 250,000, so they are present in the ratio of sixteen or twenty erythrocytes to one blood platelet.

In ordinary preparations of blood they usually form little groups (Pl. 32, Fig. 81). Each platelet is a spherical corpuscle about 3 μ in diameter. In

its center is a granular substance which is considered by many writers to be a rudimentary nucleus. The substance of the corpuscle shows a slight affinity for basic dyes, while the granules are more strongly basophilic. They never contain hæmoglobin.

When special precautions have been taken the blood platelets exhibit everywhere the form of little rods, and they are of this form in the circulating blood.

Whether, as has been claimed, the blood platelets play an important part in the coagulation of the blood cannot yet be told with certainty. The coagulation of the blood, i.e., the excretion of firm fibrin from the blood plasma, depends on the presence of a ferment, the fibrin ferment, which is present in the blood and, according to the views of many authors, in the blood platelets as **thrombogen.** Outside of the vessels **kinase** is provided by the leucocytes, which changes the thrombogen into **profibrin ferment,** that furnishes with the lime salts of the blood the fibrin ferment.

The Hæmokonia

There remains to be mentioned a final morphological element of the blood which has been discovered very recently by means of the ultramicroscope, the hæmokonia, or blood dust. These are always in very lively dancing motion, and probably are not all of the same nature. In many cases they are granules of fat, the number of which seems to be increased enormously after a full meal.

Physiological Importance and Replacement of the Corpuscular Elements of the Blood in Adults

The erythrocytes carry oxygen to all parts of the body. It is for this purpose that they are provided with hæmoglobin, which unites with oxygen in the lung to form oxyhæmoglobin, and gives it up in the capillaries to the tissues and their cells. The transportation of carbonic acid produced in the tissue cells is also cared for in part by the erythrocytes, with the hæmoglobin of which the gas may unite, but the bulk of the latter is carried in the venous blood combined with the constituents of the blood plasma.

The erythrocytes are being used up constantly during life. They die and are broken to pieces chiefly in the spleen, bone marrow, and lymphatic glands, where their remains are seized upon by special leucocytes, the **macrophagi,** and transformd into pigment, which is the matrix of the biliary coloring on the bone marrow.

The replacement of the dead erythrocytes devolves exclusively on the bone marrow, where new ones originate from the so-called **normoblasts,** i.e., cells from 6 to 12 μ in diameter, that contain nuclei and hæmoglobin, but lose the former through pycnosis. For more concerning this subject, see the chapter on the bone marrow.

The leucocytes also have important duties in the economy of the body, the most important of which depends fundamentally on their power of ***amœboid movements,*** that enables them not only to change their places, but

also to seize upon foreign bodies, in other words to act as **phagocytes.** The neutrophilic leucocytes and the large mononucleated, nongranular transition forms are the principal ones that undertake the duties of phagocytosis, and are known as **microphagi** and **macrophagi.** They are able to seize upon and render harmless not only the products of disintegration in the body itself, but also foreign elements, like bacteria, parasites, and particles of carbon. Substances of a ***fermentative*** nature also are formed in the bodies of the leucocytes and perform various duties, such as the ***breaking up of fat, the digestion of albumin, oxidation,*** and ***reduction.*** These activities are probably associated with the granulations.

Like the erythrocytes the leucocytes are constantly dying in the body and their remains being disposed of by similar cells. Replacement takes place in several places. **Lymphoblasts** are continuously formed by mitotic segmentation of the cells present in the lymphatic glands and follicles, are transformed into lymphocytes, and are carried by the lymph current into the blood. Leucocytes also develop in the bone marrow, where the erythrocytes are formed. They come from cells that are identical with the lymphoblasts of the lymphatic glands and are known as **myeloblasts;** these diminish in size and first become **myelocytes,** which, with the elaboration of specific granulations and a characteristic transformation of the nucleus, provide the various kinds of granular leucocytes. The bone marrow cannot be said not to furnish lymphocytes, although it is chiefly concerned in the production of granular leucocytes, neither can the lymphatic glands be held to purvey lymphocytes exclusively, for granular leucocytes originate in them, though in comparatively small numbers. Another place where leucocytes develop is the spleen, in which both granular and nongranular white blood corpuscles are produced.

Up to the most recent times a great difference of opinion prevailed concerning the origin of the blood platelets, but now it may be regarded as certain that they also come from the bone marrow, where they are produced by the constriction of large cells, which we shall learn to know as giant cells in the description of that organ.

2. THE BLOOD VESSELS

The blood vessels develop with their contents, the blood, from the mesoderm as a common matrix, as we have seen in the preceding chapter. The most peripheral cells of the blood islands lie close together and unite to form an epithelium, and thus give rise to a much branched space in the wall of the vitelline sac that is closed on all sides, the **primitive blood vessel.** The separate blood islands unite, but at the same time send out *shoots*, by segmentation of the epithelial cells, which are at first solid but soon become hollow through separation of their cells. These shoots anastomose, so that finally the entire wall of the vitelline sac is permeated by a dense network of young blood vessels. From the vitelline sac the vessels pass over into the embryonal body, though blood vessels are also formed independently in this.

At first the entire vascular system of the embryo consists of such primitive vessels arranged in a plexus, then individual trunks become further differentia-

ted, others disappear, and the final condition gradually develops. During this time the vessel wall undergoes typical changes. The **vascular epithelium,** which originally consisted of only a single layer of cells, is later strengthened by the surrounding mesenchymatous cells that envelop it like a sheath, and the primitive becomes the **secondary blood vessel.** These are the stellate cells, the processes of which anastomose. Wherever large trunks are to be formed the mesenchymatous sheath gradually becomes stronger, its cells lodge more densely and become transformed, part into ***smooth muscle cells,*** part into ***collagenous*** and ***elastic fibers,*** until the vessel is enwrapped externally to the epithelium by a sheath consisting of smooth muscle fibers, connective tissue, and elastic tissue, which we call the **tunica media,** while the epithelium forms the **tunica intima.** Outside of the media then appears a second sheath composed principally of connective tissue, the **tunica adventitia.** The intima has about the same structure in all vessels, but the media and adventitia not only differ quite materially in the arteries and veins, but in both present typical variations according to the size of the vessels and its position in the body.

The Capillaries

The capillaries have the original construction and plexus like arrangement of the secondary blood vessels of the embryo completely preserved; i.e., they consist simply of an epithelial tube, the **tunica intima,** enveloped by a cellular **adventitial sheath** (Pl. 33, Figs. 83 and 84).

The cells that constitute the intima of the capillaries are very thin, elongated, irregular plates, so arranged that their long diameters lie in the longitudinal direction of the vessel (Pl. 33, Fig. 84). The usually oval nucleus bulges the thin cell body into the lumen. The individual cells are joined together very firmly by a cement which is stained black by silver salts. Wherever several cells come together this cement is frequently massed into a larger quantity.

The adventitial sheath consists of stellate cells, the processes of which anastomose and interweave about the epithelial tube. They are contractile, and are able to so compress the tube by their contraction as to cause the lumen to completely disappear.

The Arteries

In contrast with the capillaries the three layers of the walls of the arteries can always be demonstrated, with the exception only of the transition places from arteries into capillaries, the so-called **precapillary arteries,** the walls of which are like those of the capillaries but for the presence of a network of fine elastic fibrils between the epithelium and the adventitial sheath.

The intima of the arteries consists, as in the capillaries, exclusively of the epithelial tube, which presents about the same picture in all and is composed of long, irregular cells. The epithelial cells are shorter in the largest arteries than in the medium sized and small. Their long axes, as well as those of their ovoid nuclei, lie longitudinally with the direction of the vessel (Pl. 34, Figs. 85 and 86).

Much greater differences may be found in the **media,** the most important component of which is formed of ***smooth muscle fibers,*** which in general have a circular course, so that their longitudinal axes are perpendicular to the longitudinal axis of the vessel. As the nuclei of these cells are likewise fairly long we now have two kinds of nuclei in the arterial wall, those that are placed longitudinally, the epithelial nuclei, and those that are placed transversely, the muscular nuclei. In the smallest arteries the muscle fibers of the media are at first pretty separate, surrounding the epithelial tube like rings, but very soon they unite to form a continuous layer, and then are placed in several layers, one upon another. Generally speaking we may say that the thickness of the musculature increases with the caliber of the vessel, yet we can distinguish among the larger arteries those that are strong and those that are weaker in muscular tissue. Among the former are the femoral and radial arteries, among the latter is the carotid. But the musculature gradually recedes into the background in the largest arteries, so that the aorta and the pulmonary artery are destitute of it at the places where they originate.

Elastic tissue plays an important part in the media. It appears, as we have seen, in the precapillary arteries, and increases continuously with the caliber of the vessel until finally it completely displaces the muscular tissue (Pl. 35, Figs. 87 and 88). The elastic tissue is found in the media in the form of nets which are mainly arranged concentrically, so that they are to be seen in the cross section of the vessel usually as very tortuous, circular lines. The elastic network finally becomes changed to an elastic membrane, as its meshes become smaller until their only remaining traces are numerous apertures, such as we meet with chiefly in the large arteries. These elastic networks and membranes lie everywhere between the muscular fibers, enveloping and separating them. The two alternate in the large arteries, a layer of muscular fibers with an elastic lamella (Pl. 35, Fig. 88).

One elastic lamella, which we call the **elastica interna,** is particularly strong in all arteries, even the smallest (Pl. 35, Figs. 87 and 88). It is very tortuous and lies just beneath the epithelium in small arteries. In the medium sized vessels it is separated from the epithelium by a longitudinally striated, delicate layer containing elastic fibrils, within which scattered muscular fibers may be detected in the aorta. The muscular fibers therefore occur between the interna and the elastica interna. Formerly not only the epithelium, but also this layer and the elastic interna were included in the term intima.

Besides the circular network of elastic fibers we meet with in the media **radiating elastic fibers,** but these are always absent in the cerebral arteries and in the aorta. They may run through the entire thickness of the media in either straight or curved courses, may furcate, and usually pass over into the elastic interna. Many authors believe these fibers to be the dilatators of the arteries.

In addition to the elastic tissue we find in the media between the muscle fibers a **collagenous tissue,** connective tissue cells and fibers.

The greatest part of the adventitia of the arteries consists of **collagenous connective tissue,** the bundles of which run chiefly in a longitudinal direction, but also take a circular course in the inner portion. Between these bundles

are nets of elastic fibers, which are often very coarse, and are placed most densely at the margin of the media, where they form a sort of elastic limiting membrane, called the **elastica externa** (Pl. 35, Fig. 88). The elastic networks are developed most strongly in the adventitia of the medium sized arteries and gradually disappear in the largest. The adventitia also contains ***muscular tissue*** in the form of little bundles of smooth fibers running longitudinally, which never form coherent masses, but are always scattered about. They appear first in the medium sized arteries and are absent in the largest. The adventitia of all arteries blends without any sharp demarcation with the connective tissue surrounding the vessels.

The Veins

The well-known macroscopical differences between the wall of a vein and that of an artery are that the former is the thinner in vessels of the same size, and that it does not increase in strength in the same proportion to its caliber. Valves also are developed in veins, though not in all, which prevent a reflux of the blood current. The thinner condition of the venous wall is essentially due to a weaker development of the media, while the adventitia is usually thicker than that of the artery, but a sharp delimitation of the two is very rarely possible.

The epithelium does not differ from that of the artery.

The **media** is weakly developed, is entirely absent in many veins, like the vena cava superioris, and even where it is strongest it is only a weak layer of circular, smooth muscle fibers associated with bundles that run longitudinally. Between the muscle fibers are networks of elastic fibers, but these by no means attain the magnitude of those in the wall of the artery, and never form true elastic membranes (Pl. 35, Fig. 89; Pl. 36, Fig. 90). An **elastic interna** can usually be made out, but it is never anything more than a fine fibrous network. In the majority of the larger veins it rests directly on the epithelium, but in those of medium size a longitudinally striated connective tissue may be interposed, and in the veins of the lower extremity, especially in the vena dorsalis penis, bundles of smooth muscle fibers run obliquely or longitudinally internal to the elastica interna.

The media passes over without any demarcation into the **adventitia,** which forms the lion's share of the entire wall of the vein, and always contains a considerable quantity of ***muscular tissue,*** consisting exclusively of bundles of smooth muscle fibers running longitudinally. They usually lie scattered about, separated by richly developed collagenous connective tissue, but may unite to form a continuous longitudinal muscular layer (Pl. 36, Fig. 90). The adventitia is extremely rich in **connective tissue,** the bundles of which run in all directions, some circularly, some obliquely, some longitudinally, cross and interweave together. Elastic tissue is scanty in the adventitia of the veins and is found chiefly in the form of delicate networks about the muscle bundles.

The **valves** are duplicatures of the wall of the vein, in the construction of which the intima and media take part, but not the adventitia (Pl. 35, Fig. 89). The epithelium on the peripheral, convex side is the same as that of the

intima of the vein, but that on the central, concave surface, the one toward the heart, is composed of irregular polygonal cells. The elastica interna extends from the wall of the vein in undiminished strength over the peripheral surface of the valve, yet ends at its margin, is wholly absent beneath the epithelium of the central surface, and reappears gradually at the base of the valve. The musculature of the media shows at the base of the valve a not inconsiderable thickening, and extends for a very little way into the valve itself, yet the muscular bundles disappear very soon so that by far the greater part of the valve is free from muscular tissue and is composed exclusively of bundles of connective tissue, part of which take a circular, part a radiating course, with some scanty elastic fibers between them.

The Vessels and Nerves of the Blood Vessels

The walls of the capillaries and of the small arteries and veins obtain their nutrition from the blood coursing through the vessels, but those of the larger arteries and veins have their nutriment supplied by special vessels known as **vasa vasorum,** which come from neighboring blood vessels, run in the adventitia, and penetrate with their capillaries into the media (Pl. 35, Fig. 88).

All blood vessels are supplied by ***nonmedullated fibers from the sympathetic nerve,*** which weave about the capillaries in wide meshes and form in the walls of arteries and veins three plexuses that are connected together. First comes a **plexus fundamentalis** in the adventitia; then a **plexus perimuscularis** at the border between the adventitia and the media; and finally a **plexus intramuscularis** in the media. The fibrils coming from the last attach themselves with little end bulbs to the muscular fibers. The vessel wall also contains ***medullated sensory fibers,*** which likewise form a plexus in the adventitia, from which extend delicate fibers that become nonmedullated and spread out in the border toward the media in end organs like antlers.

3. THE HEART

The development of the heart follows the same course in principle as that of the blood vessels. It starts from two masses of cells paired on each side of the middle line in the most causal portion of the rudimentary head between the mesoderm and the entoderm. Each of these are grouped like epithelium and form little tubes, from which grow the primitive vessels, just as in the blood islands. When the foregut closes itself these two heart rudiments gradually approach until they finally blend and furnish the single heart tube. This last consists exclusively of the epithelial tube, but soon the cells of the visceral wall of the cœlom protrude from the heart rudiment into pleuropericardial cavity, the so-called **cardiogenous plate,** apply themselves closely to the epithelial tube and differentiate themselves into striated muscle cells. In time a powerful muscular mantle is formed about the rudiment of the heart, which is now passing through its well-known process of metamorphosis. Outside of this lies the epithelium of the pericardial cavity, so that now we can distinguish three different layers of the heart: the innermost the **epithelium,** or **endo-**

cardium, derived from the vessel cells; outside of this the **musculature** or **myocardium,** derived from the wall of the cœlom and developed to very different degrees of power in the various parts of the heart; and outside of this an epithelial layer which represents the epithelium of the cœlom itself, the **epicardium** (Pl. 36, Fig. 91).

The **endocardium** lines the entire inner surface of the heart and has when fresh either a reddish, or an almost pure white appearance, as in the left auricle and on the valves, with every possible shade between these two extremes. Its most important constituent is the ***cardiac epithelium,*** but in addition we include in the endocardium the tissue on which the epithelium rests and which join it to the myocardium.

The **epithelium** of the heart is directly continuous with that of the vessels entering or leaving, and differs in no way from it. Next to the epithelium is a layer of connective tissue which is developed to different degrees in different parts of the heart, and in which elastic and smooth muscle fibers evolve mainly in postembryonal life. The elastic fibers form networks and increase in thickness from within outward. The smooth muscle fibers run in the endocardium as scattered bundles, or unite into denser bands, as in the wall of the septum in the left ventricle. Externally to the elastic network lies a layer of connective tissue which is commonly known as the **subendocardial tissue.**

The **myocardium** forms by far the greatest part of the substance of the heart and consists mainly of the ***cardiac muscle fibers*** already described, which unite to form a meshwork, or wickerwork, as we have seen (Pl. 28, Figs. 71 and 72). The cardiac muscles arise from a connective tissue supporting apparatus that may be called the **skeleton of the heart,** which includes the ***annuli fibrosi*** of the atrioventricular valves and of the mouths of the arteries, the ***septum membranaceum,*** and the ***trigona fibrosa.*** It is the province of descriptive anatomy to depict these formations and the arrangement of the muscle of the auricle and ventricle, so we shall deal only with their minute structure.

The **skeleton of the heart,** which may be cartilaginous or even bony in the lower animals, is composed in man of a dense connective tissue that is permeated with fat cells. A ***vesicular supporting tissue*** also appears between the masses of connective tissue in the trigona.

The **muscle fibers** of the heart unite first into small bundles, which in turn form either thicker fasciculi or single layers. They are separated and encased by loose connective tissue in which numerous elastic fibers are to be found, that can scarcely be perceived in the newborn, but always become more powerful in the course of life in response to the functional demands made upon the muscles (Pl. 36, Fig. 91). The connective tissue also enters into the primary bundle and surrounds each muscle fiber with a delicate envelope.

The musculature of the ventricles is independent of that of the auricles, and the two are united only by a system of muscular fibers known as **His's bundle,** or the **atrioventricular bundle.** This can be distinguished macroscopically from the rest of the musculature of the heart, from which it is separated by a strong connective tissue sheath. The muscular fibers themselves are richer in sarcoplasm and poorer in fibrils than those of the rest of

the muscles, and also contain less glycogen. At their commencement in ***Tavara's nodes*** the fibers lose their identity and pass over into the musculature of the auricle, while in the musculature of the ventricle they lose themselves in ***Purkinje's threads,*** which are much less prominent in man than in many mammals, but are characterized by their greater abundance of sarcoplasm and their marginal fibrils.

The **valves** of the heart consist of a connective tissue foundation covered by the endocardium on both sides (Pl. 37, Fig. 92). This lamina fibrosa of the valve is poor in elastic fibers, while the valvular endocardium is permeated very strongly with elastic networks. The ***atrioventicular valves*** in the embryo are almost entirely muscular, but in the adult the muscular tissue, though present, is much reduced in quantity. The ***semilunar valves*** contain no muscular elements, but consist wholly, with the exception of the epithelial coat, of connective tissue, the fibers of which run in various directions with finer or coarser elastic fibers between them. The ***noduli*** of the margin of the valve are produced by a deposit of fat in the connective tissue.

The **epicardium** forms the outer covering of the heart and passes over on to the large vessels in the pericardium. Toward the pericardial cavity it is covered by a single layer of low polygonal cells, the ***epicardial epithelium,*** which rests on a layer of connective tissue that contains many elastic fibers and passes directly into the adventitia of the large vessels at the places where they are given off. The epicardium is joined to the myocardium by a connective tissue that is developed to different degrees in different places, the ***subepicardial tissue,*** which is continuous with the connective tissue of the myocardium. A development of fat takes place in this, especially at certain places of predilection, such as the sulcus coronarius and the sulci interventriculares.

The **pericardium** has a structure quite like that of the epicardium, and like it presents toward the pericardial cavity a single layer of ***epithelium*** consisting of rather higher cells. Beneath the epithelium lies a connective tissue permeated with elastic networks, which in turn is joined to the neighboring organs by a ***subpericardial*** connective tissue containing fat.

The heart is supplied with blood through the two **coronary arteries,** which were formerly thought to be terminal arteries, but it is known now that both they and their branches anastomose freely. The arteries and their larger branches run first in the subpericardial connective tissue, then penetrate into the myocardium, lying here in the connective tissue septa, and finally break up into capillaries which enmesh the muscle fibers. The veins that carry away the blood generally accompany the arteries and are without valves, except where they empty into the coronary sinus.

The **lymphatics** of the myocardium surround the cardiac muscle fibers as cleft-shaped hollow spaces that gather together into little vessels which run between the muscle bundles and empty into the larger lymph channels that accompany the blood vessels. The endocardium and epicardium likewise contain lymphatics which form extensive networks in the subendocardial and subepicardial tissue. Little lymphatic glands may also be found in the course of the lymphatics in the subepicardial tissue.

The **nerves** of the heart come from the ***cardiac branch of the vagus***

and the ***cardiac nerves of the sympathetic,*** which unite to form the ***cardiac plexus.*** From this comes the coronary plexus, which accompanies both of the coronary arteries. From this coronary plexus, which lies beneath the epicardium, the nerves enter the wall of the heart together with the blood vessels, and form an extensive network in the epicardium, myocardium and endocardium, which enmeshes the muscle fibers in the myocardium. Fibers extend out from this plexus to end on the muscle fibers with little end bulbs. We also find sensory endings in the heart in the form of terminal tufts with many twigs in the connective tissue of the myocardium, endocardium and epicardium.

The plexuses of cardiac nerves are plentifully provided with **ganglia** (Pl. 37, Fig. 92). They are to be found in the coronary plexus, and also in the extensions of the latter into the subepicardial connective tissue of the chambers. Each ganglion contains a varying number of capsulated nerve cells of the sympathetic type, part of the neurites of which end in the neighboring cells, while part leave the ganglia to end in more distant ganglion cells. Medullated nerves also enter the ganglion, perforate the cell capsules, and end in the ganglion cells.

4. THE LYMPH

The lymph is a fluid that coagulates like blood spontaneously outside of its vessels. It comes from various sources, the tissues, the serous cavities, and the chyle of the intestines. Like the blood it consists of a **plasma** with **corpuscular elements** suspended in it. The latter are ***lymphocytes,*** which the current of lymph is carrying to the blood, where we have already become acquainted with them. Together with them we find, though much more sparsely, ***transition forms*** and ***neutrophilic leucocytes.***

The lymph plasma also contains minute particles of fat brought to it in the chyle from the intestines, and is the fat absorbed for nutrition. When the quantity of fat is small, as during fasting, the lymph is almost as clear as water, but when the quantity is great, as after a full meal of fatty food, it is milky in appearance.

5. THE LYMPHATICS

The blood vessels form a completely closed system of cavities, but the same cannot be said of the lymphatics, for their beginnings, or roots, frequently are clefts in the connective tissue of such organs as the skin. Here belong also the serous canaliculi of the cornea. The lymphatics at their beginnings also form sheathlike spaces about the blood vessels, as may be seen very beautifully about those in the Haversian canals of bone, and those of the iris. The secretory parts of many glands are surrounded in a similar way by such lymph sheaths. The roots of the lacteals of the intestines are closed cavities with which we shall become better acquainted in the study of the intestinal villi. From these **roots** the lymph flows into very narrow channels, the **lymphatic capillaries,** which form an extensive, large meshed plexus. The lymphatic capillaries are quite like those of the blood in their structure, with the exception that the lining epithelium is always composed of larger cells. They have no valves.

Small lymphatics are formed by the confluence of the lymphatic capil-

laries, and have a connective tissue envelope added to the epithelium. Very soon smooth muscular fibers appear in it, and then its structure is quite similar to that of a small vein. We can distinguish an **intima,** a **media,** and an **adventitia,** but these are very imperfectly separated. Beneath the epithelium is a thin layer of connective tissue permeated with network of elastic fibers. The media is poorly developed and contains muscular fibers that run in a circular course, together with some scanty elastic fibers. The adventitia consists mainly of bundles of connective tissue running longitudinally, with smooth muscle fibers, likewise running longitudinally, in the ***larger lymphatics*** and the ***thoracic duct,*** but never in such thickness as in the large veins.

The lymphatics, like the veins, are provided with **valves** to prevent a reflux of the lymph stream, but they are more delicate and are situated much more closely together.

The larger lymphatics are supplied by special little **blood vessels** and nerves. Nonmedullated nerve fibers surround them with a very dense plexus lying in the adventitia, from which delicate fibers extend into the media and end on the muscle fibers.

6. THE LYMPHOID ORGANS

Organs are inserted in numerous places in the lymphatic system where they must be passed by the lymph stream, which provide for the lymph its corpuscular elements and also serve as a sort of filter to arrest any foreign bodies that may have entered the lymph stream.

The simplest of these lymphoid organs is the **lymphatic follicle,** or **solitary follicle,** roundish or ovoid bodies enclosed in a more or less distinct connective tissue **capsule.** The interior of the latter is filled with ***reticulated tissue,*** the meshes of which often show a distinct concentric arrangement, particularly in the periphery, and are filled with lymphocytes. The lymphocytes are most scanty in the periphery of this adenoid tissue just beneath the capsule, so as to leave a narrow interstice known as the **lymph sinus.** In the center of the node appears the so-called **germinal center,** where the lymph cells become larger, the nuclei brighter, and many mitoses are always to be found; in other words, where the replacement of the cells continually removed from the lymph stream passing through the follicle takes place. The lymphatic enters on one side of the lymph sinus and passes out of the other, so that we may look upon the sinus as a dilatation of the lymphatic.

Such **solitary follicles** are found in numerous places in the human body, especially in the various mucous membranes.

When several solitary follicles unite they form an **aggregated follicle,** such as we find in the mucous membrane of the digestive tract, as follicular glands in the tongue, as tonsils in the fauces, and as Peyer's patches in the intestines.

The **lymphatic glands,** or **lymphatic nodules,** present a further development of the purpose of the follicles. Like them they are interpolated in the current of lymph and chyle, and, as a result of their labyrinthine structure, the lymph is kept longer in the gland, is filtered better, and is given more opportunity to become loaded with lymphocytes (Pl. 37, Fig. 93).

Each lymphatic gland is encased in a capsule that consists mainly of reticulated tissue in which elastic fibers are to be found. This capsule sends processes, **septa** and **trabecula,** from place to place within the organ, that soon unite so as to form a layer of little chambers open toward the center. Toward the interior of the gland these chambers run out into tubes which anastomose and form a network. Thus both the peripheral chambers and the central system of tubes are separated by the trabecula sent out from the capsule. The trabecula consist of reticulated tissue, like that of the capsule, and are strengthened by the blood vessels which run in them.

The lymphatic gland is commonly shaped more or less like a bean, so that we may distinguish a convex and a concave surface. On the latter the capsule appears to be drawn in, and here it penetrates into the interior of the organ so that the peripheral layer of chambers is absent. At this place, which is known as the **hilus of the gland,** the blood vessels enter the organ and then course within the trabecula.

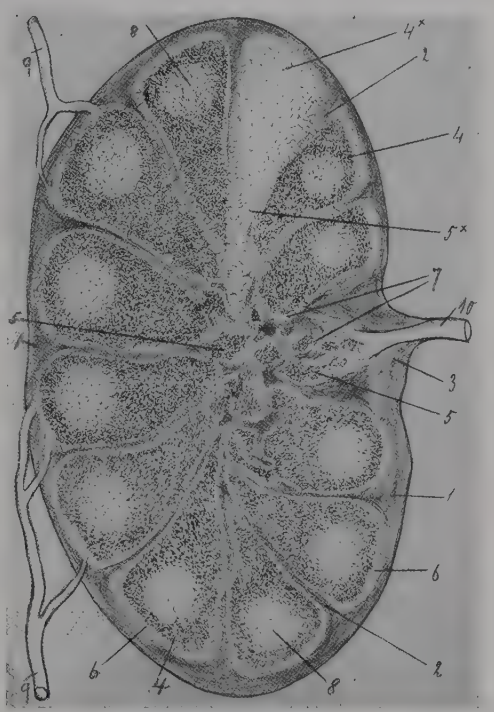


Fig. 29.—Schematic Picture of the Structure of a Lymphatic Gland.

1, capsule; 2, trabeculum; 3, hilum; 4, cortical follicles; 5, medullary cords; 6, superficial lymph sinus; 7, deep lymph sinus; 8, germination center of the cortical follicles; 9, vasa afferentia; 10, vas efferens.

The system of hollow spaces formed by the trabecula and bounded externally by the capsule, is filled by the **parenchyma** of the lymphatic gland. This consists peripherally of more or less roundish masses, the **cortical follicles,** which taper off toward the interior of the gland into the so-called **medullary fasciculi,** or **lymphoid cords,** which unite and form a framework, the **medulla** of the lymphatic gland, that is separated from the capsule by the cortical follicles and comes in contact with it only at the hilus.

The parenchyma is nothing else than adenoid tissue, i.e., reticulated tissue infiltrated with lymphocytes. The processes of its cells and its collagenous fibers join the capsule on the one hand, the trabecula on the other, but the most peripheral portions, those parts directly adjoining the capsule and the trabecula, are not infiltrated with lymphocytes, so that both the cortical collicles and the lymphoid cords are separated from the capsule or trabecula by larger or smaller interspaces through which pass the fibers of the reticulum. These spaces form the **lymph sinus,** of which there are two parts, the superficial and the deep. The structure of the cortical follicles is like that of the solitary follicles. Each has a **germinal center,** where lymphoblasts are formed by segmentation of the cells present (Pl. 38, Fig. 94).

The paths of the lymph stream through the lymph sinus are now clearly

marked out. The entering lymphatics, **vasa efferentia,** usually are several little trunks that approach the convex surface of the gland, perforate the capsule, and pour their lymph into the superficial lymph sinus situated between the capsule and the cortical follicles. From here the lymph courses toward the center until it reaches the deep sinus about the lymphoid cords. From this labyrinth of fissures it gathers finally in the neighborhood of the hilus, where the sinuses come together, and form a little vessel, the **vas efferens,** which leaves the gland at the hilus. The lymph stream in passing through the gland thus has to pass through not only a very long, but a very narrow channel, so that it is furnished the most abundant opportunity to load itself with lymphocytes, and at the same time to get rid of the foreign bodies it has been carrying.

7. THE SPLEEN

The structure of the spleen coincides with that of the lymphatic glands in so many points that we may consider it as a lymphatic gland interpolated into the circulation of the blood. It is like them of purely mesodermal origin, and it appears first as a conical thickening of the dorsal mesogastrium. This rudiment remains undifferentiated for a long time, until an outer capsule and an inner framework is developed with the entrance into it of the blood vessels. Then follows a marked growth of the organ, which forms an important center for the development of the red blood corpuscles during a certain period of embryonal life.

Like the lymphatic glands the spleen is enveloped in a **capsule** which sends numerous ***trabeculæ*** into the interior of the organ (Pl. 38, Fig. 95). The capsule is adherent to the peritoneum and consists of a dense connective tissue permeated with elastic networks, and also containing smooth muscle fibers. The spleen likewise has a hilus, where the capsule enters the organ along with the blood vessels.

The capsule sends processes, called **trabeculæ,** from its entire inner surface into the interior of the organ where they unite in an irregular manner. The trabeculæ have the same structure as the capsule and carry the blood vessels in the same way as those of the lymphatic glands.

The **splenic pulp** corresponds to the parenchyma of the lymphatic glands. It is an adenoid tissue traversed by numerous blood vessels, and fills the entire space within the capsule and the framework. But while we meet with lymphoblasts and lymphocytes almost exclusively in the parenchyma of the lymphatic glands, we find here other elements, entirely aside from the cells of the reticulum. First, there are **red blood corpuscles,** both normal and dying, and their remains. Then come **lymphocytes** and **macrophages,** with their bodies stuffed with these remnants. In the spleen of embryos and of children we also find the nucleated rudiments of the red blood corpuscles and giant cells, such as we find in adults only in the red bone marrow.

The erythrocytes present give the splenic pulp a dark red appearance in which punctate white portions stand out in relief. This is the **adenoid tissue** of the spleen, which has no erythrocytes and presents a quite typical and intricate arrangement, intimately associated with the course of the blood vessels. We will therefore turn our attention first and briefly to these.

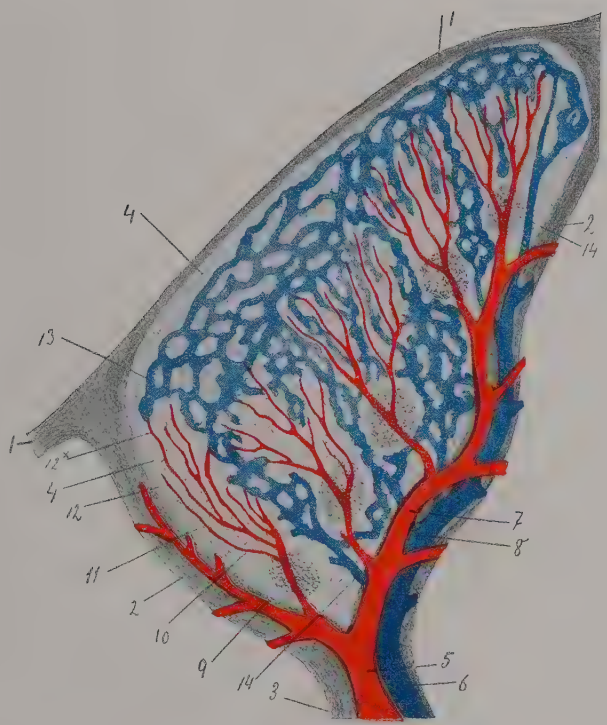


FIG. 30.—Schematic Picture of the Structure of the Spleen.

1, capsule; 2, trabeculum; 3, hilum; 4, pulp; 5, artery; 6, vein; 7, trabecular artery; 8, trabecular vein; 9, Malpighian corpuscle; 10, penicillate artery; 11, capsular artery; 12, arterial capillaries that open into the pulp; 12*, arterial capillaries that open into a splenic sinus; 13, splenic sinus; 14, pulp vein.

The **arteries** of the spleen enter the organ at the hilus together with the **veins,** ramify, and always course in the trabecula, from which they do not emerge until their diameter has diminished to about 200 μ. Each twig is soon surrounded, usually at a place of branching, with a sheath of adenoid tissue, which appears as a little, roundish nodule about 0.5 mm in diameter, that is macroscopically visible and is known as a **Malpighian corpuscle** (Pl. 39, Fig. 97). The arteries coming from the corpuscles soon decrease greatly in caliber and break up into quite a number of minute twigs known as the **penicillate arteries** or **penicilli.** Each penicillate artery is invested after a prolonged course with a theca of fibers running longitudinally. The **thecal artery** is very short and is marked by the fact that its epithelial cells project strongly into the lumen. Very soon it loses the theca and becomes an **arterial capillary** which opens into the splenic sinuses. The sinuses form a mesh of medium sized blood spaces throughout the entire pulp of the spleen and give off the veins of the pulp, which assemble into the veins of the trabecula that accompany the corresponding arteries. The splenic sinus is lined with a quite peculiar epithelium consisting of long, so-called **rod cells,** the nuclei of which project far into the lumen, while from their cell bodies come ledgelike projections that run longitudinally, and others that take a circular course and interlock with the former in grooves (Pl. 38, Fig. 96). Another conception is that these ledges are fibers that have become independent of the rod cells, so that longitudinal and circular fibers have to be distinguished. Spaces are left between the cells or the fibers through which the sinus communicates with the pulp.

The space between the sinuses of the spleen is filled with the adenoid, loose tissue of the **pulp.** This contains a system of cavities into which a part of the arterial capillaries open, and between which and the sinus many communications exist, so that two ways are open for the blood current to take through the spleen, one directly through the arterial capillaries into the sinus, the other more troublesome and affording more resistance, from these capillaries through the pulp into the sinus. In both cases the veins of the pulp and of the trabecula care for the outflow. This arrangement makes the spleen an important factor in the *regulation of the circulation of the blood* in the abdominal cavity.

In addition to this the spleen is beyond doubt an important *center for the development of lymphocytes,* known also as **splenocytes,** in extrauterine life. These originate in the adenoid tissue and reach the sinus, part by diapedesis, part through the direct communications. In intrauterine life the spleen is also an important center for the development of erythrocytes, but this function ceases after birth, and then the spleen serves as a *place for the annihilation of erythrocytes,* which break down in the pulp and are seized by the macrophages. The hæmoglobin thus set free is carried by the blood current to the liver and there transformed into biliary pigment.

The spleen is extremely well supplied with **nerves.** By far the majority of these are nonmedullated fibers, yet medullated ones are to be found amongst them. They accompany the blood vessels, enter the pulp with them, and form dense plexuses about the arteries, the veins and the sinus. Sensory nerve endings may also be made out in the spleen, especially in the trabecula, which explain how swelling of the spleen may cause severe pain. The nonmedullated fibers are exclusively for regulating the dilatation and contraction of the vessels.

II. THE DIGESTIVE ORGANS

1. THE LIPS

The **lips** bound the oral fissure, which is the entrance to the digestive tract. They are covered externally by the skin of the face, internally, toward the vestibulum oris, by the mucous membrane of the mouth. These coverings shade into each other in the oral fissure, in which the transition portion is brought out in strong relief to the skin by its red color. We may thus distinguish in a cross section of a lip a ***cutaneous,*** and a ***mucous membranous portion,*** separated by striated muscles that serve to move it, the ***muscular stratum*** (Pl. 44, Fig. 108).

The **skin** of the lip is like that of the rest of the body, which will be described in a later chapter, with certain characteristics of its own. The **epithelium,** or **epidermis,** is a stratified flat epithelium consisting of a few layers of cells, the outermost of which are horny. The epidermis rests on a connective tissue **corium,** which, contrary to the rule elsewhere on the surface of the body, contains only a very slight development of papillæ. In it lie many sweat glands, hair bulbs, and sebaceous glands, which are particularly evident in males. Internally to the corium is the loose connective tissue of the subcutis, the **subcutaneous tissue.**

These conditions change at the place where the skin passes over into the **transition portion,** in that the hair bulbs and sweat glands disappear, while the sebaceous glands remain, at least in a large percentage of the cases. At the same time the thickness of the epithelium gradually increases through multiplication of the layers of cells, and the cornification of the outer layers decreases, so that the epithelium becomes more transparent and allows the contents of the subjacent, extremely well developed blood capillaries to show through. The layer of connective tissue beneath the epithelium, which we must now call the **tunica propria,** corresponding to the corium of the skin, shows a distinct development of papillæ, though they are still quite inferior.

The transition into the true **mucous membrane of the mouth** takes place at a greater or less distance in different individuals, and is characterized by a still thicker epithelium, atrophy of the sebaceous glands, entire disappearance of cornification, and greater prominence of the papillæ.

It may be well at this point to elucidate briefly what is meant by a mucous membrane. We understand by a **mucous membrane** the lining of a cavity that communicates with the surface of the body, which, as its name implies, secretes a fluid mucus in many, though not in all cases. This secretion keeps the membrane moist and gives it its typical softness and lubricity. The mucous membrane is covered by an ***epithelium*** differing in structure in different cases, which rests on a ***tunica propria,*** consisting either of collagenous connective

tissue, or of reticulated tissue, and forms crests or ***papillæ*** that project into the epithelium. Between the epithelium and the propria there is often interposed a ***membrana propria,*** or ***basal membrane.*** Next to the propria commonly follows a ***tunica submucosa,*** which unites the mucous membrane proper with the musculature, or with its bony or cartilaginous substratum, and consists of loose connective tissue. In the submucosa, or in the propria, lie glands that open on the surface of the mucous membrane. When these glands are large and massive they often are removed far from the vicinity of the mucous membrane and are then united with it by long excretory ducts.

To return now to our subject, the **mucous membrane of the lips,** and of the mouth as well, is quite generally covered by a stratified flat epithelium in which there are many layers of cells. It never shows cornification except on the tongue. The **propria** is a purely connective tissue formation in the mouth and is composed of interwoven and decussating connective tissue fibers. It forms **papillæ** that often, especially near the transition portion, project deeply into the epithelium, but without causing the latter to protrude in adults. In newborn infants, on the contrary, the epithelium itself forms such papillæ, or villi, which naturally have a papilla of the propria as a basis over which they form an epithelial covering.

In the connective tissue **submucosa** of the lip, that now follows, lie numerous glands, the **glandulæ labiales,** corresponding to the glandulæ buccales of the mucous membrane of the cheek. Both are compound branched alveotubular glands. Their fairly wide excretory ducts usually pass obliquely through the propria to the epithelium and open in the depression between two papillæ. In the submucosa the excretory duct enters the true gland, which lies here in the form of a large, distinctly lobulated mass, divides into many interlobular branches, from which a twig enters each little lobule, where it breaks up into the intermediate portions that lead to the ***terminal chambers, some of which are serous, some mucous.*** These glands bear a close resemblance to the sublingual gland, which may be referred to for further details.

The **muscular stratum** interposed between the skin and the mucous membrane consists of the fibers of the orbicularis oris. They follow a circular course about the oral fissure and therefore appear cut across in a cross section of the lip. They are striated muscular fibers of medium thickness gathered into larger and smaller bundles. The stratum bends like a hook at the place of transition and ends about where the cutaneous portion begins. In addition to those that unite to form bundles, we always meet with numerous isolated fibers in the subcutaneous tissue, and between them fibers either alone or in bundles that have been hit longitudinally, which therefore pass obliquely through the lip from without inward. They also appear everywhere between the bundles of the orbicularis oris, wind between the glands, and reach the propria of the mucous membrane. These are known in their entirety as the compressor labii.

The supply of **blood vessels** varies in different parts of the lip. It is least in the cutaneous portion, most abundant in the transition and mucous membrane portions. The superior labial or coronary artery and vein of the two sides anastomose and form a corona vascularis internal to the muscular stratum

in the submucosa near the inner angle of the lip, from which twigs pass to the two portions and form wide meshed plexuses in the subcutis and submucosa. Still finer twigs extend from these to the corium and the propria. Each papilla of the corium or propria contains a minute arterial twig, which breaks up there into capillaries that reunite in one or more little veins.

The **lymphatics** form a cutaneous and a submucous network that communicate in the transition portion. Numerous little trunks assemble from these networks and lead to the submaxillary, superior cervical, and submental lymphatic glands.

The lips are supplied by both motor and sensory nerves, through the facial and the trigeminal. The former ends on the muscle fibers, the latter partly free in the epithelium of the skin and mucous membrane, partly in special end organs in the subcutis of the type of *Krause's* and *Vater-Pacini's* corpuscles.

The structure of the cheeks is so familiar to that of the lips that no further description is necessary.

2. THE TEETH

The **teeth** are hard organs that are phylogenetically nothing else than ossified cutaneous papillæ, such as we find very extensively in the skin of the lower vertebrates. Ontogenetically they develop from two different parts of the mucous membrane of the mouth, the epithelium and the connective tissue of the propria.

The first rudiment of a tooth appears in a thickening of the epithelium which extends deeply along the margin of the embryonal jaw in the form of a crest, the **tooth band.** Corresponding superficially to it is a furrow along the mucous membrane of the jaw, the **dental groove.** The epithelium for the formation of each tooth dips in deeply in the form of a cone that is rather club-shaped at its end. A proliferation of connective tissue grows about the base of this club, separates it from the neighboring connective tissue, and thus converts the epithelial cone into the dental sac, the connection of which with the tooth band is still preserved. The peripheral parts of the dental sac then proliferate more deeply into the tissues, while the epithelium covers the connective tissue about the base as a cap on a head, so now we are able to distinguish two parts of the dental sac,—the epithelial covering, or **enamel organ,** and a mass of connective tissue with a broad base in the interior, the **dental papilla,** which is directly continuous with the subjacent connective tissue.

There are ten such dental sacs in each of the upper and lower jaws, one for each milk tooth. While the dental sac hangs at first like a pear on the epithelial stalk, the latter gradually moves down later to the inner side of the sac and develops there a second clublike thickening, the **rudiment of the permanent tooth.** As soon as this is formed the stalk separates from the sac and dies, together with the tooth band.

About the beginning of the fourth month of the human embryo important changes take place in the further enlargement of the dental sac, now lying in

the deep part of the mucous membrane covering the alveolar margin, part of which goes to form the enamel organ, part the dental papilla.

While the enamel organ consists at first of the same kind of epithelial cells, a differentiation now becomes noticeable. The peripheral cells join closely together into a single layer of epithelium, while the central ones assume on the contrary the character of mesenchymatous cells, move apart, become stellate, anastomose with their processes, and secrete a gelatinous substance between themselves. Thus we have two parts of the enamel organ, the **enamel epithelium,** and the **enamel pulp** enclosed by the former. In that portion of the enamel epithelium that lies directly on the surface of the papilla the cells are long and cylindrical, while those that cover the enamel pulp above are always lower and flatter. We call the former the **enamel cells,** and their entirety the **enamel membrane,** or the **inner enamel epithelium,** while the latter is known as the **outer enamel epithelium.**

Changes take place at the same time in the dental papilla. The connective tissue cells that lie just beneath the enamel cells separate themselves from the others of the papilla, elongate into long, cylindrical elements placed together like epithelium, and bound on all sides the substance of the papilla toward the enamel membrane. These are known as the **odontoblasts.** Thus we have now in the dental sac two epithelial caps, one over the other, the upper of which, the sac supposed to be standing upright, originates from the epithelium of the mouth and therefore from the ectoderm, the lower from the connective tissue of the mucous membrane of the mouth and therefore from the mesoderm.

From these two epithelia comes the hard substance of the tooth, which makes its first appearance about the end of the fifth month of embryonal life. *The odontoblasts secrete the greater part of this, the dentine, the enamel membrane, and the smaller part of the enamel.* The **dentine** is secreted by the odontoblasts in the form of a mass that is at first structureless and is deposited between them and the enamel membrane. The odontoblasts grow with processes in this **predentine.** Each cell sends out a process that is frequently branched, which grows with the increase of the predentine, passing through its entire thickness. Collagenous fibers very soon appear in this predentine, running parallel to the surface of the dental rudiment, and then calcification begins and advances from within outward, changing the predentine into dentine. The dentine forms a constantly thickening mantle about the dental papilla, which assumes the shape of the complete tooth, so that finally the papilla comes to lie in a little cavity in the tooth, the **pulp cavity,** and is joined to the subjacent connective tissue by the narrow **root canal,** which passes through the lower, projecting segment of the dentine, the **dental root.** In the young tooth what was the papilla forms the contents of the pulp cavity, the **pulp,** the most superficial cells of which are odontoblasts.

The development of the **enamel** sets in somewhat later than that of the dentine. First each enamel cell excretes from its surface a **cuticula,** from which a process extends toward the dentine, **Tomes's process;** it calcifies and is separated from its neighbor by a richly developed **cement.** The calcification advances with a gradual reduction of the enamel cells to the outer surface, and changes each enamel cell into a long, prismatic, calcified formation, the

enamel prism, which stands about perpendicularly to the surface of the dentine. The young enamel prisms are separated from one another by an abundant **cement,** which gradually disappears as the prisms continue to grow. The entire enamel membrane does not take part in this formation of enamel, only the portion surrounding the upper segment of the dental rudiment, which later becomes the **crown of the tooth.** Below the inner and outer enamel epithelia begin to draw together at an early period with atrophy of the enamel pulp, and the farther the development of the enamel advances the more does this approximation progress upward, until finally the entire enamel pulp is obliterated and even the remains of the enamel epithelium are destroyed. Of the cells of the enamel membrane the cuticula alone is preserved, which after birth covers the young enamel as a continuous layer, the **cuticula dentis.**

A third tissue is added to the dentine and enamel in the first month of life, the **cement,** which is a bony substance secreted by the connective tissue about the root of the tooth.

We have therefore to distinguish in the complete tooth:—a, The **dentine,** which forms the main part of the entire tooth and encloses the ***pulp cavity*** and the ***root canal,*** but never appears on the surface; b, the **enamel** which covers the dentine like a cap, is thickest above, gradually becomes thinner until it ceases at the neck of the tooth, and therefore is present only over the free crown of the tooth projecting from the gums where it is covered by the ***cuticula dentis;*** c, the **cement,** which begins where the enamel ceases, covers the entire root with a thin layer, and extends to the beginning of the root canal, the foramen apicis; d, the **pulp,** which fills the cavity of the tooth. To these may be added e, the **periodontal membrane,** and f, the **gums.** We will briefly discuss each of these in turn.

a. The Dentine

We can differentiate a dentine of the crown and a dentine of the root. Its structure can easily be understood from what has been said concerning the embryology of the teeth. The **basal substance** consists of collagenous fibrils which run parallel to the inner surface of the tooth, but cross in all possible directions. They form numerous layers one over another and are not calcified themselves but are held together firmly by a calcareous cement. Within this basic substance uncalcified places are to be found in the crown dentine near the border between the enamel and the dentine in the form of irregular cavities, the **interglobular spaces,** into which the calcareous basal substance projects with roundish knobs, the **dentine globules.** The interglobular spaces in the crown dentine are quite large and form a continuous layer parallel to the border of the dentine enamel; in the dentine of the root they are much smaller, but have the same position and arrangement, and here form **Tomes's granular layer** (Pl. 43, Figs. 104 and 105).

The basal substance of dentine is permeated by **dental tubules,** or **canaliculi,** which radiate from the pulp cavity to the margin of the enamel or cement in such a way that they run almost exactly transversely in the root and always obliquely upward. They are so dense as to give the dentine a char-

acteristic striated appearance. Where they open into the pulp cavity they have a diameter of 4 or 5 μ, which gradually diminishes as they give off numerous fine lateral twigs through which both neighboring and distant canaliculi form many anastomoses. They divide dichotomously sooner or later, and have blind ends at the enamel dentine margin, or form arching connections. Part of them pass this border and end in the enamel with a little swelling. The interglobular spaces are permeated by the canaliculi, which frequently end in the dentine of the root in Tomes's granular layer (Pl. 43, Figs. 104 and 105).

The basal substance forms particularly resistant sheaths about the canaliculi and their twigs, just as in bone, the so-called **Neumann's sheaths.**

b. The Enamel

The **enamel** is the hardest organic substance of all animal tissues and contains the least water. It is composed of **enamel prisms** bound together with **cement.** The prisms are not of uniform thickness, but become thicker from the dentine to the outer surface (Pl. 43, Fig. 106). In the cross section they are pretty regularly pentagonal or hexagonal, and are indistinctly striated in the longitudinal section. The substance of which they are composed is doubly refractive. As the enamel prisms pass through the entire thickness of the enamel in screwlike windings they are never met with throughout their entire length in a section, but only in short transverse or oblique segments. In the longitudinal section of a tooth dark lines appear in the enamel which are known as the **striæ of Retzius** (Pl. 42, Fig. 103; Pl. 43, Fig. 104). In the neighborhood of the neck they run obliquely to the surface of the dentine, but the farther up we go in the tooth the more acute becomes the angle formed, until they are almost parallel just over the top of the dentine. **Schweger's striæ,** which appear as horizontal parallel lines on the surface of the enamel, do not change in this way; they are to be seen as transverse bands in the section.

The surface of the enamel is covered by the **cuticula dentis,** or **enamel cuticle.** This is, as we have already seen, the original cuticle of the enamel cells, is extremely resistant, calcified, structureless, and attains a thickness of only 1 or 2 μ.

c. The Cement

All parts of the outer surface of the tooth that have no enamel, that is, the neck and the root, are covered by the **cement,** which usually extends a little way over the enamel (Pl. 42, Fig. 103). Its thickness increases from above downward and is thicker on the permanent than on the milk teeth. It originates from the connective tissue about the dental sac in the way we learned in the study of bone substance, and therefore consists of a fibrillary, stratified ***basal substance,*** in which are placed ***bone cells*** with numerous offshoots enclosing ***bone cavities*** (Pl. 43, Fig. 105). The thinner the layer of cement, the more sparse are the bone cavities, which are almost entirely wanting in the region of the neck. ***Haversian canals*** may also be met with in old, thick cement. ***Sharpey's fibers,*** with which we became acquainted in the study of bone, may be seen very distinctly in the cement passing vertically through the lamellæ of

the basal substance that run parallel to the surface. They appear in the section of the macerated tooth as little hollow tubes.

d. The Dental Pulp

The **pulp** fills the **pulp cavity** and the **root canal** or **canals,** and consists of connective tissue richly supplied with vessels and nerves (Pl. 44, Fig. 107). It contains numerous fine, decussating connective tissue fibers with very many stellate connective tissue cells between them. Toward its surface the tissue becomes richer in cells, denser, and finally consists next the dentine of a coat of long cylindrical cells, the **odontoblasts.** These cells send out several fine processes into the pulp, where they are lost, and each cell also sends a long fiber to the dentine, the **dentine fiber,** or **Tomes's fiber,** which enters a canaliculus and extends in it a long way.

The **blood vessels** that enter the pulp through the root canal course through its middle and send branches to the periphery, where a dense capillary network is formed which reaches into the layer of odontoblasts.

The pulp is also supplied with **lymphatics,** that gather into several little trunks in the root canal and leave it to enter the maxillary or deep cervical glands.

The **nerves** accompany the blood vessels, branch and form a wide meshed plexus within the pulp from which fibers extend, after losing their medulla, to form a second plexus within the layer of odontoblasts. Minute fibrils from this penetrate the dentine with the dentine fibers and form there a third plexus, which again sends fibers to the border between the dentine and the enamel, or the cement, where they end with little clublike thickenings. No nerves exist in the enamel or the cement.

e. The Periodontal Membrane

By the **periodontal membrane,** or the **periodontium,** we understand the tissue that joins the root of the tooth to the alveolus and its neck to the gums. It consists mainly of connective tissue fibers, part of which extend transversely, part obliquely between the parts mentioned. They are inserted at one end into the cement of the root, at the other into the bony substance of the alveolus, where they appear as Sharpey's fibers. The intermediate space is filled with a loose connective tissue containing blood vessels and nerves.

f. The Gums

We call that part of the mucous membrane of the mouth the **gums** which covers the alveolar processes of the jaws, clothes the neck of each tooth that protrudes from the alveolus, and forms a fold over the septa interalveolaria between every two teeth. The gums are firmly united to the periosteum of the alveolar process by its subcutaneous tissue, and are also connected with the neck of the tooth through the periodontal membrane. Its structure is in general that of the mucous membrane of the mouth already described, from which it

differs in having high papillæ of the propria, and in the total absence of glands. It is richly supplied with blood vessels and sensory nerves, and possesses a very extensive lymphatic network within the propria.

3. THE TONGUE

The **tongue** is substantially a muscular organ that develops in the floor of the mouth from four separate rudiments, two of which are paired and two are not, that appertain to the ventral ends of the first three branchial arches. These rudiments unite, the two paired ones forming the body, the others the root of the tongue, which is phylogenetically the older portion. The musculature, which for the most part belongs to the postbranchial myotome, then invades this connective tissue and epithelial rudiment from behind. We have therefore to consider first the ***mucous membrane*** with the ***submucosa,*** and then the ***musculature.***

The **mucous membrane** of the tongue resembles on the whole that of the lips and cheeks, yet displays characteristic differences. In the anterior portion of the front part of the tongue the papillary development attains a magnitude found nowhere else in the mouth. The part lying behind the sulcus terminalis, the after part of the tongue, has on the contrary no papillæ. We meet with high papillæ in the propria of the mucous membrane of the lips and especially of the gums that are always covered so smoothly with epithelium as to scarcely appear superficially, but in the mucous membrane of the tongue the papillæ are so high as to project above the surface as pointed or fungus shaped elevations. These papillæ may be divided according to their shape into filiform, fungiform, circumvallate, and foliate.

The **filiform papillæ** are spread uniformly over the entire front part of the tongue, rise with broad bases out of the propria, and either simply run to a point, or form a sort of socle or base from which the slender, secondary acuminate papilla projects (Pl. 45, Fig. 109). Such a socle may support as many as twenty secondary papillæ. They stand very close together in the mucous membrane, have a quite pale or grayish color, and give the surface of the tongue its peculiar velvety appearance.

The **fungiform papillæ** are usually shorter. The slender body is thickened above so that the papilla looks like a club, or a mushroom (Pl. 45, Fig. 109). Here also secondary papillæ project from a papillary base, yet the epithelium passes smoothly over them and fills more or less completely the intervening depressions, so that the secondary papillæ can scarcely be seen externally. The fungiform papillæ differ from the filiform not only in their shape, but also in their color; they are always bright red, and are scattered over the back of the front part of the tongue, more numerous in the anterior than in the posterior parts.

The **circumvallate papillæ** are found only in small numbers, seven to twelve, at the line of demarcation between the front and back parts of the tongue, arranged in the form of an obtuse V open forward, the apex of which lies in the foramen cæcum. They are inverted, broad, truncated cones, the smaller parts of which are sunken deeply into the mucous membrane so that

the bases, 1 to 2 mm broad, look upward and are placed in the plane of the surface of the mucous membrane (Pl. 45, Fig. 110). The latter forms about the papillæ a low wall which is separated from it by a deeply cut, circular groove. The surface of the circumvallate papillæ is studded with low secondary papillæ which do not project externally.

The **foliate papillæ,** which are rudimentary in man, are found in the back part of the margin of the tongue as several low folds that run obliquely to the surface of the tongue and are separated by slight furrows. Each fold is studded with numerous secondary papillæ. On the back part of the tongue the place of the papillæ is taken by the **lingual follicles,** roundish or elongated, flat elevations of the mucous membrane that may be as much as 4 mm in diameter. They have in the middle a little opening which leads into a short, blind canal, usually running obliquely to the surface.

The **epithelium** of the mucous membrane of the tongue is of the flat variety and is composed of many layers. It covers all of the papillæ, dips into the sulci about the circumvallate papillæ, and lines the cavities of the lingual glands. Its most superficial layers are ***cornified*** where they pass over the filiform papillæ. The outermost horny cells give these papillæ the gray color that contrasts with the color of the fungiform papillæ which are not horny. These horny cells, which are constantly being cast off and appear in large masses in the saliva, form very large, flat elements that often take the form of little cones stuck into one another.

Another characteristic of the epithelium of the tongue is the appearance of peculiar budlike formations, which are the end organs of the glossopharyngeal nerve and are known as **taste buds** (Pl. 45, Fig. 110; Pl. 92, Fig. 197). Although these are found in all of the fungiform papillæ of fetuses and infants, they are confined in adults mainly to the epithelium of the lateral surface of the circumvallate papillæ and the opposite surface of the surrounding sulcus. They also occur in the epithelium of the foliate papillæ. Their structure will be described when we come to speak of the organ of taste.

The **propria** of the mucous membrane of the tongue consists of a dense connective tissue containing many cells. It forms the main part of the papillæ. In the region of the lingual follicles it undergoes an important alteration in that ***lymph follicles*** are embedded in it, and the connective tissue changes into reticulated tissue, the meshes of which seem to be stuffed with lymphocytes. Quite a number of such follicles lie in each of the lingual follicles, where they lie closely together and surround the cavity of the sac with a complete lymphoid mantle just beneath the epithelium. Lymphocytes wander continually from the follicles through the epithelium into the cavity of the lingual follicle, where they seem to be destroyed.

The **submucosa** of the tongue joins the mucous membrane and the musculature, and is continuous with the connective tissue of the latter. On the dorsum of the tongue the connective tissue is greatly developed and has received the name of fascia linguæ. The ***lingual glands*** lie in the submucosa, frequently reaching inward to between the muscular bundles. They are distributed very unevenly over the after part and the posterior portion of the fore part of the tongue, leaving the anterior three quarters of the latter free, except for

a small area in the middle line of the apex, where they form near the under surface the ***Blandin-Nuhn's,*** or ***anterior lingual glands.***

The great bulk of the lingual glands, particularly all of the posterior ones, are *purely mucous,* and belong to the compound branched alveotubular type. The excretory ducts open either on the surface of the mucous membrane, or in the cavities of the lingual follicles, are lined with cylindrical epithelium, traverse the propria, and reach the lobes of the gland situated in the submucosa. A branch of the efferent duct enters each lobule, breaks up into many twigs, and terminates in the end chambers lined by high cuboidal mucous cells.

Serous glands, or **Ebner's glands,** are found only beneath the circumvallate and foliate papillæ, where taste buds are present (Pl. 45, Fig. 110). They are compound branched tubular glands. Their excretory ducts, likewise lined with cylindrical epithelium, open in the floor of the groove surrounding the papillæ, branch in their course through the submucosa, and change into the end tubules in the gland. The end tubules are lined with a single layer of cuboidal or conical cells, between which many secretory capillaries are to be found. The cells elaborate a secretion rich in albumin, the initial stages of which distend their bodies with fine granules.

The **Blandin-Nuhn's** is a ***mixed*** gland, the structure of which is just the same as that of the sublingual gland, which will be described later.

The **musculature** of the tongue consists of striated muscle fibers that appertain to the outer and inner muscles of the tongue (Pl. 45, Figs. 109 and 110). Among the former are the hyoglossus, the genioglossus, and the styloglossus; among the latter are the longitudinal, transverse, and vertical lingual muscles. These muscles are so arranged that in a cross section of the tongue part of the bundles are seen running from above downward, part from right to left, and part cut transversely. They are imperfectly separated by the median septum linguæ, composed of connective tissue, into right and left halves, and they end in the fascia linguæ.

Part of the **arteries** of the tongue extend to the muscles, part enter the submucosa and thence supply the mucous membrane. They form a rich arterial plexus from which twigs extend on the one hand to break up into long capillary meshes about the muscle fibers, on the other into the propria where they form capillary loops in the papillæ just beneath the epithelium. The glands also are enmeshed by a well developed capillary plexus. The **veins** formed by the confluence of the capillaries follow the same course as the arteries.

Networks of lymphatics are found both in the propria and its papillæ, and in the submucosa, the efferent trunks of which lead, some to the cervical, some to the lingual lymphatic glands.

The **nerve supply** of the tongue is very complicated. The hypoglossus furnishes all of the muscles with motor twigs which terminate in end plates on the striated muscle fibers. The nerve of taste is the glossopharyngeal, the lingual branches of which penetrate to the submucosa of the back part of the tongue and the region of the circumvallate and foliate papillæ, where they form a large plexus from which nerves extend to the mucous membrane. Part of the fibers end free in the epithelium, part form another plexus about the taste buds

from which twigs enter each. The glossopharyngeus also sends out gustatory fibers by way of the minor superficial petrosal nerve, the otic ganglion, and the chorda tympani, which reach the anterior part of the tongue in company with the sensory fibers of the lingual branch of the trigeminus. The sensory fibers in turn form a plexus in the submucosa from which fibers rise into the papillæ, where some terminate in the epithelium, and others enter special end corpuscles within the papillæ, part of which are of the Vater-Pacini, part of the Krause and Ruffin type of construction. The glossopharyngeus is the secretory nerve of the lingual glands.

Small **ganglia** occur in the plexus formed by the sensory nerves of the tongue, consisting of a few cells that belong to the sympathetic type.

4. THE PALATE

The **hard palate,** that separates the mouth from the nasal cavity, is covered by a mucous membrane the characteristic feature of which is that it is very firmly and tightly joined to the periosteum, especially in its anterior portion. It differs in no way from that of the lip. **Palatine glands** are to be found in the submucosa; they are most abundant in the posterior part, become more and more scanty as we pass forward, and are completely absent in front of the bicuspids. Like the glands of the posterior part of the tongue they are **purely mucous,** and their excretory ducts empty on the surface of the mucous membrane through numerous openings that are visible to the naked eye.

The **soft palate,** which is a continuation of the preceding, is a membrano-muscular fold that incompletely separates the cavity of the mouth from that of the pharynx. In front it belongs to the mouth, behind to the pharynx, and this dual nature is stamped in the structure of its mucous membrane.

The **mucous membrane of its anterior surface** is the same as that of the hard palate, like it consisting of a stratified flat epithelium and a propria having low papillæ. The papillæ become higher and denser the nearer we approach the free margin. The submucosa contains quite a layer of ***mucous glands,*** a direct continuation of the glands of the hard palate, as well as numerous ***fat cells,*** and is permeated toward the propria with dense elastic networks.

The **mucous membrane of its posterior surface** is, on the contrary, a continuation of that of the posterior nares, and like the latter is covered with stratified cylindrical epithelium provided with cilia. The transition between these two territories is not at the free margin, but on the posterior surface, so a part of the latter is covered with stratified flat epithelium. A propria with numerous high papillæ comes next to the epithelium. In the submucosa lie ***glands,*** which are not purely mucous, but are ***mixed*** and are of the type of those of the lips.

A strong **muscular layer** is interposed between the mucous membranes of the anterior and posterior surfaces; this serves to move the soft palate and consists of striated fibers. Many collections of glands enter between the muscle bundles from the anterior surface.

The **blood vessels** and **lymphatics** resemble those of the lips and cheeks. The lymphatics empty into the deep cervical glands.

The **nerves** of the palate are partly motor, partly sensory. Those that supply the muscles come from the trigeminus and from the pharyngeal plexus, the sensory nerves from the sphenopalatine ganglion.

The **tonsils** are embedded in the sinuses tonsillares between the pillars of the fauces on each side. These are nothing else than greatly enlarged follicular glands, such as are seen on the posterior part of the tongue, and may be imagined to originate from the packing together closely of from twelve to fifteen such follicles. Correspondingly the tonsil presents on its surface oval openings, each of which leads into a follicular cavity, called the tonsillar sinus, that is not simple as in the follicles of the tongue, but presents many prongs (Pl. 46, Fig. 111). Otherwise the structure is just the same as that of the lingual follicles. **Mucous glands** are to be found in the submucosa which for the most part open in the floor of the follicle cavity. The tonsil is separated from the surrounding mucous membrane by a tight connective tissue **capsule** furnished by the submucosa. Each follicle is supplied by it with a separate sheath that reaches to just beneath the surface.

The **lymphatics** form in the tonsil a very dense plexus between the individual follicles, with branches leading into each, and empty into the deep cervical glands.

5. THE SALIVARY GLANDS

The large salivary glands of the mouth, the **submaxillary, sublingual,** and **parotid,** develop like the small glands of the mucous membrane from eversions of the epithelium. A solid cone of the latter grows down into the tissue and, after it has reached a certain length, sends out lateral branches from place to place, which in turn send out more sprouts, until they finally end in terminal buds. This glandular trunk is at first solid, but becomes hollow later by a separation of its epithelial cells, and then through a differentiation of these, becomes divided into an excretory and a secretory system. At a very early period a capsule is formed about the gland rudiment from the surrounding connective tissue, that is at first purely cellular. It forms septa that separate the terminal regions of the excretory ducts and divides the entire rudiment into numerous lobes. The connective tissue cells also lie about the excretory ducts and end pieces of the gland rudiment and surround them with a basketlike envelope.

The **secretion** of the large salivary glands, together with that of the glands of the mucous membrane, forms the ***saliva,*** a viscid, frothy fluid as clear as water, of neutral or slightly alkaline reaction, made up of 9.4% organic, 0.6% inorganic matter, and 99% water. Among the former constituents are the salivary mucin, an albuminoid, ferments, oxydase, and sulphocyanate of potassium. The most important of the ferments is ptyalin, which changes starch into dextrin and sugar, and thus transforms a large part of the food into a soluble form in which it can be absorbed. The fluid also contains morphological elements, the **salivary corpuscles,** round, rather swollen cells, in

which a nucleus cannot always be demonstrated. They contain numerous granules that exhibit Brown's molecular movement very beautifully, a condition that indicates at once that we have to deal here with dead cells. Formerly it was quite a general belief that these were lymphocytes which had been formed in the lymphoid organs of the mouth, the tonsils and the follicular glands of the tongue, as well as in similar organs in the pharynx, and had reached the mouth through the epithelium, but we know now that the greater part if not all of the salivary corpuscles are not lymphocytes, but neutrophile leucocytes which wander into the salivary glands and also into the mouth through the epithelium, where they reach the saliva, swell up and die. They furnish the saliva its oxydase, or enzymes.

We will pass now to the consideration of the individual glands.

The Submaxillary Gland

The submaxillary, the largest of the human salivary glands, is a mixed gland, i.e., its secretion is a fluid containing mucus and albumin, which is liquid and only slightly viscid.

Its **excretory duct,** which opens in the mouth close to the frenulum linguæ on the caruncula sublingualis, is a fairly thin walled duct lined with a double layer of cylindrical epithelium and encased in a sheath of connective tissue containing many elastic fibers.

The body of the gland is enveloped by a connective tissue capsule, and is divided by numerous septa into a large number of larger tertiary, and smaller secondary and primary lobes and lobules.

Within the gland the excretory duct breaks up into ***numerous branches*** which first run between the tertiary lobes and then, constantly dividing and becoming smaller, between the secondary lobules. Here the double layer of cylindrical epithelium becomes single, the connective tissue sheath gradually disappears, and the lumen contracts (Pl. 47, Fig. 114; Pl. 48, Fig. 116). When the **little excretory ducts** finally arrive in the septa that separate the primary lobules they divide again and an important change takes place in each section. The lumen dilates again somewhat and at the same time the cells become higher and cylindrical. While the cells in the little excretory ducts are almost cuboidal and are distinctly separated by boundary lines, these cells are higher and very imperfectly defined. The nucleus lies close to the lumen, and the basal segment of the cell appears to have radiating striæ. This striation is due to the fact that the cell protoplasm here forms long, radiating meshes with numerous microsomes embedded in the walls. We call this formation, which we meet with in other glandular cells as well, **Heidenhain's rods.** Near the nucleus this rod structure ceases and the entire cell body is distended by similar granules that lie so close as to completely cover the protoplasm. This part of the glandular cavity is known as the **salivary tubules.** They belong not to the excretory, but to the secretory portion of the glandular substance.

The salivary tubules, which thus lie between the primary lobules, are comparatively short and soon break up, with considerable diminution in size, into the **intermediate pieces** that enter the primary lobules and on which the

terminal chambers hang like berries on a common stem (Pl. 47, Fig. 114). These are either spherical or rather elongated, saclike, and together compose a primary glandular lobule. In the intermediate piece the cylindrical epithelium of the salivary tubule changes into a lower, cuboidal, indifferent variety, which gives place in the terminal chambers to the true **secretory epithelium.**

The latter varies in the different terminal chambers. The spherical ones are lined with cuboidal, or better conical, cells and enclose a very narrow cavity from which numerous **secretory capillaries** extend between the glandular cells (Pl. 48, Fig. 115). Roundish nuclei are to be seen in the cells, sometimes near the center, sometimes close to the base, and the cell bodies contain more or less numerous granules. When the gland is at rest they lie uniformly thick throughout the entire cell, but during its activity they become discharged into its lumen, where they very soon become fluid and are lost to sight. The granules in the cell gradually decrease, advancing from the base toward the lumen, and, when the activity is maintained long enough, a time comes when the cells are completely empty of granules. Then follows their replacement from the microsomes of the base. This proceeds from threadlike formations near the nucleus known as **basal filaments,** which are beyond doubt of a mitochondric nature. Usually the secretory activity of the gland is less intense than this, so that the discharge and new formation of granules keep pace with each other. The granules consist of a substance like albumin, certainly contain the oxydase of the saliva, and probably also the ptyalin, or its primary stages.

The elongated, saclike, terminal chambers present essentially different pictures. In them the low cells of the intermediate pieces are replaced by high cuboidal or cylindrical cells which exhibit all of the well known properties of mucous cells. At the blind ends of these mucous sacs are groups of albuminous cells arranged like hoods, which terminate the sacs and are known as **Giannuzzi's crescents.** The lumen of the saclike terminal chambers is considerably wider than that of the spherical. From its end pass out several secretory capillaries to penetrate between the crescent cells (Pl. 48, Fig. 115).

The majority of the terminal chambers composing the primary lobules of the gland in man are spherical, albuminous alveoli; the mucous ones are greatly overshadowed and there are many lobules in which they are entirely absent. The human submaxillary is doubtless a **mixed,** yet it is a ***preponderatingly serous*** gland.

Each terminal chamber is surrounded by a structureless membrana propria, but between it and the epithelium is interposed a layer of branched, stellate cells that anastomose with one another, the so-called **basket cells.** These may also be demonstrated on the salivary tubules, but disappear on the excretory ducts.

The **blood vessels** enter the gland with the submaxillary duct and on the whole follow the same course as its branches and twigs. When they arrive at the primary lobules they break up into capillaries which wind about the terminal chambers just beneath the membrana propria.

The **lymphatics** accompany the blood vessels, twisting about them, enter the primary lobules, and end in spaces that surround the terminal chambers with the capillaries that are woven about them.

The **nerves** of the submaxillary gland come from the submaxillary gan-

glion, composed of sympathetic ganglion cells, which receives sensory fibers from the trigeminus through the lingual nerve, secretory intermediate fibers through the lingual nerve from the chorda tympani, and sympathetic fibers from the external maxillary plexus. The fibers that enter the gland from it are for the most part medullated, with a few that are nonmedullated. They accompany the blood vessels and lymphatics and are furnished with numerous little sympathetic ganglia. Within the primary lobules the nerve fibers form medullated and nonmedullated plexuses about the terminal chambers, from which proceed only nonmedullated fibers that pass through the membrana propria and apply themselves with little swellings to the secretory cells. The nerves behave in quite a similar manner toward the salivary tubules.

The Sublingual Gland

After we have become intimately acquainted with the structure of the submaxillary, that of the other salivary glands may be dealt with more briefly. The **sublingual gland** consists of a large and several smaller parts which likewise have a **major** and several **minor sublingual ducts.** Like the submaxillary it is a mixed gland of compound branched alveotubular structure, and the principal differences between the two are that the parenchyma of the sublingual consists mainly of mucous terminal chambers with Gianuzzi's crescents, and that the cells of its salivary tubules have no rod structure (Pl. 46, Fig. 112). Consequently the saliva secreted by the sublingual is much more viscid, more alkaline, and less albuminous than that from the submaxillary. It contains only small quantities of ferments and oxydase.

The relations of the vessels and nerves are the same as in the submaxillary gland.

The Parotid Gland

The **parotid,** unlike the sublingual, is a ***purely serous gland.*** Its **parotid duct,** as well as the rest of its efferent system, is exactly the same as that of the submaxillary. The smallest excretory ducts change into salivary tubules with rod epithelium, and the terminal chambers are all spherical, albuminous alveoli (Pl. 47, Fig. 113).

The saliva from the parotid is consequently free from mucin, liquid, neutral, or only slightly alkaline, and abounds in albuminous ferments and oxydase.

The lobulation of the gland by the densely developed interlobular connective tissue is very prominent.

The **nerves** of the parotid come from the glossopharyngeus and reach the gland by way of the tympanic nerve, the tympanic plexus, the minor superficial petrosal, the otic ganglion, the auriculotemporal and its parotid branches, and are associated with sympathetic twigs from the plexuses about the vessels. Small ganglia are also to be found in the interlobular connective tissue. The endings of the nerves are the same as in the submaxillary gland.

6. THE PHARYNX

Conformably to its double function as the entrance for food and for air, the pharynx has a mucous membrane clothed with epithelium that differs in different places. The **nasal part,** or **naso-pharynx,** i.e., the part that is closed below by the velum during the act of swallowing and into which the posterior nares open, is lined with the ***stratiform ciliated epithelium*** of the latter, while the **oral** and **laryngeal parts** have a ***stratified flat epithelium***.

The **propria** is well developed everywhere; it contains many high papillæ in the oral and laryngeal parts, and is characterized by the great networks of ***elastic fibers*** within it, that separate it from the subjacent muscles, into which it sends interfascicular septa. **Lymph follicles** also occur in the propria of the pharyngeal mucous membrane, which coalesce in two places into tonsillar formations, the **pharyngeal tonsil** in the middle of the roof of the pharynx and the **tube tonsil** at the mouth of the Eustachian tube. Both of these resemble in their minute structure the faucial tonsil.

A **submucosa** is developed only in the laryngeal part of the pharyngeal mucous membrane, so the ***pharyngeal glands*** lie for the most part between the muscular bundles beneath the mucous membrane. These glands are found in all parts of the pharynx and the great majority of them are purely mucous, mixed glands occur only in the nasal part.

The **muscular coat** of the pharynx is composed of the constrictors and levators, which contain only striated muscle fibers. It is covered externally by a connective tissue fascia rich in elastic fibers, which is known as the fibrous membrane, or the **tunica adventitia of the pharynx**.

The pharynx receives its blood chiefly from the ascending pharyngeal artery, the branches of which supply the muscles, glands and mucous membrane. The veins as well as the **lymphatics** form a superficial, mucous membranous, and a deep, muscular plexus. The lymphatics flow into the retropharyngeal and the deep cervical glands.

The **nerves** of the pharynx come in part from the glossopharyngeal, in part from the vagus, and in part from the superior cervical ganglion, and form a plexus provided with a ganglion on the outer surface of the constrictor medius, whence fibers pass to the muscles (vagus) and the mucous membrane.

An organ that should be mentioned here occurs in the roof of the pharynx at the mouth of the canalis craniopharyngeus and is known as the **hypophysis of the roof of the pharynx**. It consists of a connective tissue capsule, which encloses a parenchyma composed of epithelial cords and tubes lined with epithelium, the cells of which are similar to those of the anterior lobe of the hypophysis cerebri. The parenchyma is abundantly supplied with blood vessels.

7. THE ŒSOPHAGUS

After the complete closure of the entodermal intestinal tube its uppermost, blind segment, which joins the ectodermal oral diverticulum by bursting through the pharyngeal membrane, consists of an epithelial tube surrounded by a thin layer of mesenchymatous cells. The primarily fairly wide lumen later becomes narrow, and is lined by a double layer of cuboidal epithelium. In consequence of a lively cell division the epithelium comes to be formed of several layers and cilia appear on the layer facing the lumen. The cylindrical ciliated cells unite into groups, between which lie areas covered with cuboidal cells without cilia. Then the entire superficial layer of cells is cast off and we have an epithelium composed of several layers of cells, the uppermost of which flatten more and more. During this time the entire section has greatly enlarged and the tube lies in folds running longitudinally. The development of glands begins in the fourth month by the invagination of the epithelium in the cranial and caudal parts in the form of branched tubes. Similar invaginations are formed later in all of the other parts of the mucous membrane. The mesenchymatous cells enveloping the epithelial tube differentiate in two directions: one to provide a connective tissue propria and submucosa, the other to form myofibrils within themselves and to surround the lower two thirds of the tube with a mantle of smooth muscle fibers. Striated muscle fibers are formed about the upper third, but at a considerably later period.

The **mucous membrane** of the œsophagus, which lies in several longitudinal folds, is lined by an extensively stratified epithelium resembling that of the mouth, but nowhere horny (Pl. 49, Fig. 117). Islands not rarely occur within this flat epithelium of simple mucous cylindrical epithelium, such as those we shall soon become acquainted with in the stomach. These places are called **islands of the gastric mucous membrane.**

The epithelium rests on a connective tissue **propria,** which forms high papillæ, and is separated from the subjacent submucosa by a layer of smooth muscle fibers (Pl. 49, Fig. 118). This we meet with here for the first time, and it will accompany us through the entire digestive tract; we call it the **muscularis mucosæ.** It appears in the uppermost part of the œsophagus in connection with the elastic membrane mentioned under the pharyngeal mucous membrane, as separate bundles of muscular fibers which soon come together and form a continuous layer.

Glands also appear in the œsophagus for the first time within the propria, for hitherto they have been met with only in the submucosa, or in the subjacent muscles. These, known as ***cardiac œsophageal glands,*** are constant only in the lowermost segment of the œsophagus, where they surround the orifice into the stomach. They belong to the branched tubular or alveotubular type. They resemble perfectly the fundus and pyloric glands of the stomach, to which we may refer for a description. They are less constant, but are to be found in the upper part of the œsophagus, particularly at the level of the lower margin of the cricoid cartilage, where they are spoken of as the ***upper cardiac œsophageal glands.*** These glands may be associated

again with the above mentioned cylindrical epithelium, which appears in the form of depressed dimples. We have then in the œsophagus true gastric mucous membrane islands which can be seen plainly with the naked eye.

Lymph follicles also appear in many places in the propria, as in the mouth and pharynx.

The **submucosa,** which is strongly reinforced by elastic networks, contains purely mucous, compound branched alveotubular ***glands,*** that may be considered a continuation of those of the mouth and pharynx. They lie in little groups which are fairly thick in the upper part of the œsophagus and gradually diminish in number downward. The excretory duct is usually dilated somewhat like an ampulla, passes obliquely downward through the propria and opens at the top of a papilla.

The **muscularis** of the œsophagus presents an inner, circular, and an outer, longitudinal layer. In the upper third it consists exclusively of striated fibers united into bundles. At the beginning of the middle third smooth fibers appear among the striated, rapidly increase in number, and soon displace the latter entirely, so that at the middle the muscularis is composed wholly of smooth fibers. The connective tissue separating the muscular bundles blends internally with the submucosa, and externally forms a strong ***fibrous membrane,*** much reinforced by elastic fibers, which envelopes the entire organ and connects it with neighboring organs.

The **blood vessels** and **lymphatics** are quite like those in the pharynx; the latter empty into the deep cervical, bronchial, posterior mediastinal, and cardiac glands.

The **œsophageal branches** of the vagus nerve form a plexus on both the anterior and the posterior surfaces of the organ, from which fibers pierce the longitudinal musculature and form a plexus between it and the circular, which contains many nonmedullated fibers and ganglia. It is analogous to Auerbach's plexus, which we shall meet with in the intestine. A second plexus, composed exclusively of nonmedullated fibers and ganglia, lies in the submucosa. The intermuscular plexus furnishes the motor fibers for the muscularis, the submucous the motor fibers for the muscularis mucosæ, the sensory for the epithelium and the secretory for the glands.

8. THE STOMACH

The **stomach,** which appears as a spindle shaped, laterally flattened dilatation of the primitive intestinal tube, is enveloped by mesenchymatous cells and lined by a double layer of epithelium, the inner of which is composed of cuboidal, the outer of cylindrical cells, and is separated from the mesenchyma by a distinct basal membrane. The surface is smooth at first, but changes soon appear that are due to an unequal growth of the epithelium and lead to the formation first of folds in the mucous membrane, and then of depressions in its surface, the **primitive gastric dimples.** The floor of each dimple is formed by a single layer of cylindrical cells, while between them the epithelium remains of two layers. Granules very soon appear in certain ones of these cylindrical cells in the floor of the dimple that stain vividly with acid dyes.

These are the **parietal cells.** While the primitive gastric dimples are still wholly epithelial, hollow branching tubes begin to press forward in the surrounding mesenchyma, while at the same time the part of the mesenchyma set apart now for the propria drives forward the epithelium toward the lumen, so that it loses its double layer and is reduced to a single layer of cylindrical cells. Thus we have now a cylindrical superficial epithelium that sinks in like a pit, from the outer end of which a **gastric gland** extends into the propria. Differences between the fundus and the pylorus are evident at an early period, in that the dimples in the latter are much deeper than in the former, but particularly in the fact that delomorphous cells do not develop in the pylorus, where the epithelium lining the primitive dimples and later the glands consists of undifferentiated cells. It is not until very late, probably about the time of birth that a differentiation takes place in these cells within the glands both of the fundus and of the pylorus, when very fine granules develop in them and they become what are known as **mother cells.** Then we have only mother cells in the pylorus glands, and both these and the delomorphous cells in the fundus glands. Yet for a long time after birth a great part of the cells remain undifferentiated, multiply by indirect segmentation, and furnish the material for new glandular and superficial cells. At the same time the cylindrical epithelium of the surface begins to become mucous.

The first trace of muscular elements in the wall of the stomach is found in embryos in the second half of the second month of pregnancy, in the form of circular smooth muscle fibers in the mesenchyma surrounding the epithelium, which soon forms a complete circular musculature. The longitudinal muscles, which lie outside of these, appear much later. The muscularis mucosæ can be distinctly perceived in the fourth month.

The gastric mucous membrane of adults increases constantly in thickness from the cardiac orifice to the pylorus. Its free surface lies in **folds,** that form meshes running longitudinally, and presents many little depressions, the **gastric dimples,** that may be seen with the naked eye. Toward the pylorus the dimples become continually wider and deeper, while the parts of the mucous membrane between them project into the lumen like villi.

The **simple cylindrical epithelium** lines the entire inner surface of the stomach, including the dimples; its cells secrete the **gastric mucus** (Pl. 50, Fig. 119). These are long cells that taper only a little toward the propria, project their rounded free surfaces into the lumen, and have distinct cement edges between their free ends. They somewhat resemble goblet cells in construction, in that they present a deep, protoplasmic portion enclosing a nucleus, and a superficial, mucous portion. In the latter are numerous granules, precursors of mucus, which swell more and more toward the lumen. This mucous portion of the cell contains two little central bodies. But the mucous cells of the gastric epithelium differ from goblet cells very characteristically in the fact that their mucous contents are not basophilic, because albuminoids are mixed in considerable quantities with the gastric mucus.

The **propria** of the gastric mucous membrane consists principally of reticulated tissue, yet true connective tissue with very fine collagenous fibers is also to be found in it. Toward the surface the reticulated tissue becomes

thickened and forms beneath the epithelium a sheetlike layer of anastomosing cells, which also embraces the glands of the propria on all sides. In the meshes of the reticulated tissue lie many lymphocytes, yet true follicles do not occur normally in the stomach. Mast cells are also met with very often in the propria.

The propria is separated from the underlying submucosa by a well developed **muscularis mucosæ,** the smooth muscle fibers of which form several intersecting layers (Pl. 49, Fig. 118), from which slender little bundles constantly separate and mount at an oblique or a right angle up into the propria to lose themselves in the ridges about the gastric dimples (Pl. 50, Fig. 119).

The propria is also the seat of the **gastric glands,** the secretion of which is the gastric juice. The latter is a specific, thin, watery fluid, the secretion of which is excited by the mere sight of food, but much more by its introduction. It contains, in addition to water, inorganic constituents and mucus, mainly **ferments** and **hydrochloric acid.** Three ferments have been discovered in it: ***pepsin,*** which dissolves albumin, ***rennin,*** which coagulates milk, and ***steapsin,*** which decomposes fats. Free hydrochloric acid is present in the gastric juice and changes the propepsin excreted by the glands into pepsin.

The gastric glands are found in the propria of the entire mucous membrane from the cardiac zone to the pylorus, and present two forms that differ in many respects, the ***fundus*** and the ***pyloric glands.***

The **fundus glands** occupy by far the greater part of the gastric mucous membrane, that of the entire body and the fundus ventriculi. They are of the branched tubular variety, each opening in a gastric dimple with a short narrow portion, the neck of the gland. Just back of its mouth the gland breaks up into two or more branches which pass through the propria in parallel, often slightly winding courses, and end with a quite small swelling just in front of the muscularis mucosæ (Pl. 50, Fig. 119). Each of these tubes may be subdivided into a body and a fundus. These glands are aggregated very closely, as many as 100 have been counted to the square millimeter, so that the propria forms only thin septa between them.

The lumen is widest in the neck as a continuation of the gastric dimple, contracts in the body to a narrow fissure, and broadens again into a slight dilatation at the fundus. The cells that line the tube are of two kinds. Some are generally medium sized cuboidal cells that lie along the entire length of the tube and increase in size with hunger. These we know as **chief cells.** They receive their characteristic imprint from the fairly coarse granules they contain, which stain with basic dyes, the same as the chromatin of the nucleus. The general opinion is that these granules, which are difficult to preserve, are the initial stages of pepsin, the propepsin, so that of the two principal constituents of the gastric juice the pepsin is secreted by the chief cells (Pl. 50, Fig. 120).

The second kind of cells found in the epithelium of the fundus glands is the **parietal.** They differ from the chief cells in being considerably larger, and of a spherical or pyriform shape. They are not distributed uniformly in the epithelium like the others, but are aggregated much more closely in the upper part of the gland than in the lower, and may be entirely absent in its fundus (Pl. 50, Fig. 119). Exceptionally a parietal cell wanders into the epithelium of the gastric dimple. They press in as it were from without between the chief

cells, but frequently do not reach the lumen of the tube, and then are connected with it by a narrow pedicle. Another and more important difference is shown by their staining, as, unlike the chief cells, they have a strong affinity for acid dyes. The cell body contains quite minute, dustlike granulations that stain rather darker than the protoplasm (Pl. 50, Fig. 120). The secretion of hydrochloric acid is ascribed to the parietal cells, chiefly because the acid appears only in the parts of the mucous membrane where parietal cells are to be found. Up to the present time the acid itself has not been demonstrated in the cells.

Minute lateral canaliculi branch from the lumen of the fundus gland, each one of which enters a parietal cell and here forms a capillary basket in the peripheral layer of cells, the branches of which are very minute during hunger, but are thick and coarse during digestion. These **basket capillaries** are beyond doubt the tubules through which the secretion of the parietal cells escapes (Pl. 50, Fig. 120).

The **pyloric glands** are found only in the pyloric region, where they are not aggregated so closely as the fundus glands, but are separated by large trabeculæ of the propria. They are of the branched alveotubular variety. The neck develops from the gastric dimple, which here is usually very deep, and from this come several branching, very tortuous tubules that pass through the propria and end in a fundus that is distinctly thickened like a club (Pl. 50, Fig. 121). The course and arrangement of the glands is such that a section through the mucous membrane of the fundus differs materially from one through that of the pylorus; in the one densely packed tubes are to be seen cut longitudinally, running parallel through the propria with little propria tissue between them, in the other we find sections of tubules almost all cut transversely or obliquely, united into little complexes and separated from their neighbors by large masses of propria.

The glandular epithelium presents equally great differences, for the pyloric glands are lined with only one kind of cells. Although these differ slightly from the chief cells of the fundus glands, they resemble them in all essential particulars so that we may unhesitatingly pronounce them the same. In addition, the secretion from the pyloric part contains pepsin and no hydrochloric acid, and many transition forms between the two kinds of glands are to be found at the margin of the pyloric portion toward the corpus ventriculi.

A third variety of glands is the **cardiac,** which usually extend only a few millimeters from the œsophagus into the stomach, and give place very soon to the fundus glands. The cardiac glands are situated within the propria and are quite like the pyloric in their structure. Compound branched alveotubular glands are also found that extend into the submucosa and resemble Brunner's glands of the duodenum, which will be described later.

Outside of the muscularis mucosæ in the wall of the stomach is the **submucosa,** a very well developed connective tissue containing fat, which is continuous with the connective tissue of the muscularis.

The **muscularis** consists mainly of circular, smooth muscle fibers that form a continuous layer. It attains its greatest thickness in the pylorus. Externally to this circular muscular layer there appears in some parts of the stomach a layer of muscular fibers running longitudinally, that form a contin-

uation of the outer muscular coat of the œsophagus, and is most marked on the two curvatures (Pl. 49, Fig. 118). Finally we find on the inner side of the circular muscles fibers that run obliquely. They are best developed at the cardiac region, where they form a continuation of the circular muscles of the œsophagus, and arch from here over the sides of the body of the stomach to be lost on its greater curvature.

Outside of the muscularis lies the **peritoneum,** which envelops the stomach on all sides.

The **arteries** of the stomach come from the cœliac, course first in the subserosa, and send their branches through the muscularis into the submucosa, in which they form a large plexus. From this twigs rise into the propria and form about the glands capillary plexuses with elongated meshes that are particularly dense in the region of the glandual neck. The **veins** assemble just beneath the epithelium, run down perpendicularly between the glands, and form first a plexus on the muscularis mucosæ, from which twigs lead to a submucous plexus. The muscularis also is supplied by this submucous arterial and venous plexus.

The wall of the stomach is richly provided with **lymphatics.** Their roots form the perivascular spaces that lie about the superficial capillaries and veins, and open into independent little trunks between the glands which form a subglandular plexus outside of the muscularis mucosæ. This in turn empties into a submucous plexus, which also receives the lymphatics of the muscularis, and from which efferent vessels pass to accompany the arteries and to empty into the gastric and pancreatico-splenic lymphatic glands.

The **nerves** of the stomach come from the vagus and the sympathetic, and form an anterior, a posterior, and a superior gastric plexus. They accompany the vessels into the wall of the stomach, where they form an intramuscular plexus between the circular and the longitudinal muscles, and then a submucous plexus. Both of these are well provided with ganglia and they anastomose with each other. The intramuscular plexus furnishes the motor end fibers that terminate on the muscle fibers with little end plates. From the submucous plexus come numerous fibers that surround the glands with an extremely fine meshed plexus. They also enter between the epithelial cells and terminate on them with little swellings.

9. THE INTESTINE

In the early stages of development the intestine passes straight through the embryonal body, and, like the stomach at this time, is lined with a double layer of cuboidal epithelium and surrounded by an envelope of mesenchymatous cells. As soon as convolutions begin to appear in the intestinal tube the epithelium proliferates strongly and becomes stratified in its upper portion. Vacuoles appear in the epithelium and the proliferation becomes so great in the duodenum that the lumen becomes choked in many places. The differentiation of smooth muscle fibers in the mesenchyma surrounding the epithelial tube begins in embryos 10 to 12 mm long. These take a circular course about the tube and develop into a continuous layer of circular muscles. The epithelium placed be-

tween it and the mesenchyma now proliferates toward the latter and gives rise to longitudinally running folds. In the more caudal sections on the contrary the epithelium advances toward the mesenchyma with the formation of protrusions, the so-called diverticula, which later are drawn in again into the lumen. In the still more caudal sections of the intestine, that later become the colon, there is neither a marked formation of folds nor great epithelial proliferation. The epithelium here likewise at first consists of a double layer, but this changes early to a single layer of cylindrical cells.

By the time the embryos are 20 mm long a proliferation of the mesenchyma takes place in the small intestine, which advances in the form of fingerlike processes toward the epithelium, creating protrusions in the mucous membrane of the intestinal cavity, which is now open again everywhere; we know these as villi. Beginning in the most cranial portion of the intestine their development constantly proceeds toward the caudal end, so that in embryos 50 to 60 mm long the inner surface of the entire small intestine from the stomach to the colon is covered with villi, the number and development of which steadily decreases from the cranial to the caudal end.

Between the villi the epithelium runs down forming simple, straight tubes. These are Lieberkuehn's glands. In addition we find in the cranial sections the formation of special protrusions that are developed in connection with the pyloric glands of the stomach and are branched like them. We call these Brunner's glands.

Signs of differentiation begin to appear in the mesenchyma between the circular muscles and the epithelium in embryos 100 mm long. The smooth muscle fibers of the muscularis mucosæ appear in it and divide the propria from the submucosa. The former changes into reticulated tissue, in which lymphoid follicles develop in many places, while the submucosa forms collagenous fibrils and becomes loose connective tissue. Shortly before the advent of the muscularis mucosæ longitudinal smooth muscle fibers appear outside of the circular muscles, which gradually come to form a longitudinal muscular layer that is not continuous throughout the entire length of the intestine.

We have thus in the intestinal wall of adults most internally the **mucous membrane,** consisting of ***epithelium*** and ***propria,*** and separated from the ***submucosa*** by the ***muscularis mucosæ.*** Then comes the **musculature** of the intestine, composed of inner, circular, and outer longitudinal muscles. Finally the intestine is invested by the **peritoneum** throughout its entire length.

Although there is no doubt that a certain amount of absorption takes place in the upper part of the digestive tract, in the mouth, pharynx, œsophagus, and stomach, yet the intestine is the organ in which **absorption** reaches its acme. In order to provide the most extensive possible absorptive surface in the least space its mucous membrane is in the first place thrown into ***folds,*** and in the second is provided with the numerous protrusions we have just been studying, the ***villi.***

The **folds of the intestinal mucous membrane** are the **Kerkring's folds,** or **valves,** or the **valvulæ conniventes,** crescentic elevations running vertically to the longitudinal axis of the gut, that reach their greatest height

opposite the insertion of the mesentery and gradually grow less toward the latter (Pl. 51, Fig. 123). They begin about 5 mm from the pylorus, reach their greatest development in the jejunum, and disappear entirely in the lower part of the ileum. The **plicæ semilunares** take the place of Kerkring's folds in the colon (Pl. 52, Fig. 124).

The **villi** furnish a far greater increase of surface than the folds. Like them they are elevations of the mucous membrane, the form of which varies in different parts of the intestine. Above they are broad and leaf-shaped, below their breadth gradually decreases until they finally become finger-shaped. They also decrease in number from above downward and disappear entirely in the lower part of the ileum. None are to be found in the colon or rectum. The number present in the entire intestine has been calculated to be over ten millions. Experimental researches on animals have shown that the number and shape of the villi depend to a great degree on the kind of food, whether vegetable or animal. Between the bases of the villi lie the mouths of Lieberkuehn's glands.

As regards the structure of a villus, we can distinguish a body and an investing epithelium (Pl. 52, Fig. 125). The **body of the villus** is an elevation of the propria of the intestinal mucous membrane, and consists like it of reticulated tissue. On its surface the reticulum is thickened into a sort of membrane from which meshes extend essentially in a radiating direction to the axis of the villus. The latter is occupied by a lymph space, the **central chyle vessel,** or **lacteal,** into the epithelial lining of which the cells of the reticulum continue.

In the meshes of the reticulum one always meets with a large number of leucocytes, transition forms, and especially **macrophages** that come from the latter. Mast cells and eosinophile cells are less numerous.

Besides blood vessels, the course of which will be described later, the body of the villus contains **smooth muscle fibers.** They branch out of the muscularis mucosæ, just as in the propria of the stomach, several little bundles to each villus, in the body of which they form by anastomosis a very wide meshed network, and are inserted with somewhat thickened ends into the limiting layer described above. A very fine **homogeneous basal membrane** is interposed between this limiting layer belonging to the reticulum and the epithelium. The simple, cylindrical **villous epithelium** forms at the same time the superficial epithelium of the mucous membrane throughout the greater part of the small intestine, as the villi are so extremely dense. It is composed of long, prismatic cells, polygonal on section, that taper as they go down and rest with their small ends on the basal membrane (Pl. 8, Fig. 26; Pl. 52, Fig. 125). Distinct intercellular spaces remain between the cells, especially in the deeper parts, and are closed at the surface with cement edges. Intercellular bridges also may be observed between the individual cells. Each cell contains an ovoid nucleus situated in its basal third, and nucleoli can always be plainly seen. The cell body consists of a hyaline or finely granular protoplasm, vacuolized in the portions adjacent to the lumen, in which very distinct fibrils appear. These pass through the cell body in a spiral course, surround the nucleus, and become invisible in the basal parts. Just beneath the free surface lies a double central body, and we find mitochrondria here as well as in the opposite segment of the cell.

On the free surface the cells are covered by a rod band, such as has been described already in the general part of this work.

Goblet cells are to be found between these typical cylindrical cells. For the structure of these also reference must be made to the general part. They are more abundant at the bases than at the apices of the villi, in the epithelium of which may be found every transition between typical cylindrical and ripe goblet cells.

Little more remains to be said of the superficial epithelium. In the lower part of the ileum, where there are no villi, it presents the same characteristics as on those structures, except that the goblet cells become more numerous the nearer we approach the rectum. At the anus the intestinal changes quite abruptly into stratified epithelium which differs from that of the skin in that the uppermost layer of cells is cuboidal or cylindrical. This transition epithelium soon gives way to the epidermis.

The **propria** of the intestine is, as we have seen, reticulated tissue, forms the main part of the bodies of the villi, and surrounds the **glands,** or **crypts of Lieberkuehn,** which are sunk in between the villi. These crypts are simple, straight or slightly bent, short tubes that penetrate only to the muscularis mucosæ (Pl. 53, Fig. 126). They are found in the entire intestine from the duodenum to the rectum, but are much farther apart in the lower sections than in the upper, and they increase considerably in length from above downward. The lumen is comparatively wide and is lined with an epithelium that differs in only a few points from that of the surface. First, we meet with here a new kind of cell, the **Panethian,** which are cylindrical, or more often pyriform in shape, lie in the base of the gland, and are filled with fine granules that are strongly acidophilic. Probably the secretion is indebted to these cells for one of the intestinal ferments. Then we find quite small, very darkly stained cells, the so-called **peg cells,** which are collapsed Panethian cells that have lost their secretion (Pl. 53, Fig. 126). The main part of the epithelial cells of Lieberkuehn's crypts consist of superficial epithelium and goblet cells, the latter predominating considerably in the colon and rectum. Indirect segmentation is seen with extreme frequency in the epithelial cells, which probably provides for the replacement of the goblet cells that are destroyed by degrees in producing the secretion.

In the propria of the intestine are also found **lymph follicles** as little nodules lying between the glands of Lieberkuehn. They are not confined to the propria in their growth, but break through the muscularis mucosæ and penetrate into the submucosa (Pl. 52, Fig. 124). In the ileum large adenoid masses unite to form conglobate follicles, which are known as **Peyer's patches.** Here the masses reaching to the musculature are covered by a thin mucous membrane, with only scattered villi and Lieberkuehn's glands between the separate follicles, while on the top of the follicle the adenoid masses covered only by epithelium protrude into the lumen of the gut. Yet the adenoid tissue attains its greatest extent in the ***vermiform appendix,*** where the entire propria is diffusely infiltrated with lymphocytes, and we also find many solitary follicles, so that in this section of the intestine Lieberkuehn's glands suffer a great reduction and are met with only quite sporadically.

The **muscularis mucosæ** is well developed throughout the intestine. As the outer limit of the propria it passes just outside of Lieberkuehn's glands and enters into the folds, both in the small intestine and in the colon. It consists for the most part of two thin layers of muscular fibers—an inner, in which the fibers are circular, and an outer, in which they run longitudinally. Its relations to the musculature of the villi have been described above.

The **submucosa** does not attain any considerable development in the intestine. It is thickest in the upper duodenum, becomes slighter lower down, and increases again in thickness in the colon. It consists of loose connective tissue with elastic fibers, and contains glands only in the duodenum. These, known as **Brunner's glands,** are most abundant in the upper part of the duodenum, while they occur only here and there in the descending portion and are quite absent in the lower part. The large Brunner's glands alone are submucous, the small ones remain in the propria, like Lieberkuehn's (Pl. 51, Fig. 122). They are compound branched alveotubular glands, similar to the mucous glands of the mouth, but from which they differ in their epithelial lining. The mouth of the quite short excretory duct is found either between the glands of Lieberkuehn, or in the fundus of one of them. After the duct has broken through the muscularis mucosæ it breaks up immediately into quite a number of branches, which branch again and end with short alveolar dilatations. The lining of the excretory duct is a simple cylindrical epithelium, but deeper in it assumes the peculiarities of the epithelium of the pyloric glands, as may be shown by many transitions between the two kinds. Brunner's glands also contain cells that are quite similar to the Panethian cells of Lieberkuehn's crypts.

The **muscularis** of the intestine consists, like that of the stomach, of smooth muscle fibers in two layers, an inner circular, and an outer longitudinal. Both layers are well developed on the duodenum, yet the inner is three or four times as thick as the outer. Both diminish in thickness in the jejunum and ileum, but the circular musculature remains the stronger, while in the colon the longitudinal finally becomes incomplete and is confined to three thick longitudinal bands, the **tæniæ.** In the large intestine the **haustra** are formed, saclike pouches in the wall that are separated by circular furrows. The muscularis of these haustra consists exclusively of circular muscles, while they are actually produced by the longitudinal muscles, which act like short ligaments. The circular furrows, the plicæ semilunares, thus contain all of the layers of the intestinal wall and are not folds of the mucous membrane like Kerkring's folds of the small intestine. The muscularis increases again in the rectum and there attains its greatest thickness. The strong layer of longitudinal fibers passes partly into the levator, partly into the rectovesical musculature, while the circular layer becomes much thickened at the anus and forms the sphincter ani externus.

The musculature of the intestine contains much connective tissue with many elastic fibers, which extends inward into the submucosa, and outward into the subserosa of the peritoneal covering.

The **arteries,** coming from the mesenteric and the hæmorrhoidal, are situated on the whole the same as those of the stomach (Pl. 53, Fig. 127). We

have first a large arterial plexus in the submucosa from which branches extend on the one hand to the muscularis, on the other to the propria, and form a second plexus on the muscularis mucosæ. From the latter develop the capillaries that enmesh Lieberkuehn's glands closely, as well as twigs that enter the follicles, while two or three little arteries pass from it into each villus and form a capillary network in the outer layers of its body, from which the blood is collected into veins. These villous veins, together with the vessels that originate in the glandular and follicular capillaries, penetrate into the submucosa, where they form a venous plexus corresponding to the arterial. From this little trunks pass through the musculature and form with the veins of the latter a second plexus in the subserosa, from which larger trunks pass into the mesentery.

The roots of the **intestinal lymphatics** are found as perivascular sheaths about the intestinal glands, but they occur mainly in the villi, where they form the central chyle space (Pl. 52, Fig. 125). Each villus contains at least one such chyle space, and the large leaflike villi of the duodenum each contain two, which are united by transverse anastomoses. They are lined with flat epithelium and end or begin blind in the upper third of the villus. The chyle space tapers downward and appears at the base of the villus as a lymphatic or chyle vessel, takes up the perivascular lymph spaces about Lieberkuehn's glands and the lymphatic networks about the intestinal follicles, and passes through the muscularis mucosæ into the submucosa, in which a wide meshed lymphatic plexus originates that presents large varicosities. A second plexus lies between the circular and the longitudinal muscles, joined on one side with the submucous plexus, on the other with a third plexus lying in the subserosa, into which larger trunks from the submucous plexus also open directly. The chyle vessels, or lacteals, assemble finally from the subserous plexus and enter the mesentery with the blood vessels. Those of the duodenum empty into the superior and inferior pancreatic, those of the jejunum and ileum into the mesenteric, those of the cæcum and vermiform appendix into the precæcal, retrocæcal and ileocæcal, those of the colon into the mesocolic, those of the rectum into the hemorrhoidal and anorectal lymphatic glands.

The **nerves** of the intestinal canal come from the great nervous plexuses of the abdomen, the cœliac, mesenteric, aortic, and hypogastric, which belong partly to the vagus, partly to the sympathetic. They form in the wall of the intestine three plexuses that correspond to those of the lymphatics, first a subserous, then a myenteric, commonly known as **Auerbach's plexus,** and finally a submucous, commonly called **Meissner's plexus.** All three of these are united by numerous anastomoses. *Auerbach's plexus* is of coarser frame and wider meshed than *Meissner's*, as well as considerably richer in sympathetic fibers. The ganglia lie at the meeting points of the plexus and are composed of multipolar sympathetic cells. All of the fibers of the plexus are nonmedullated. Branches extend from Auerbach's plexus into the musculature and end on the muscle fibers. From Meissner's plexus fibers extend to the glands, the villi, and the entire superficial epithelium. They form fine networks that enwrap the glands and pass through the bodies of the villi. Sympathetic cells are interpolated in all of these networks.

The function of the intestine is in the first place to complete the digestion

of the food introduced that has been begun in the upper part of the tract, and then to absorb the products of this process and to supply them to the organism. It has therefore both a **digestive** and an **absorptive** function. The former is aided by the secretions of the two large intestinal glands, the liver and the pancreas, but the glands of the intestinal wall itself, Lieberkuehn's and Brunner's, provide a watery, light, alkaline fluid, known as the **intestinal juice.** This contains in addition to such inorganic substances as sodium carbonate, chloride and phosphates, **four ferments,** three of which decompose sugar, ***invertin, lactase,*** and ***maltase,*** as well as one that decomposes albumin, ***erepsin,*** and also a body known as ***enterokinase,*** which changes the protrypsin of the pancreatic juice into trypsin. The secretion of these important ferments we must describe with the intestinal glands. The amount of them in the intestinal juice constantly decreases from above downward and is nonexistent in the colon, which is not surprising, as the glands of Lieberkuehn situated here contain goblet cells almost exclusively. The question now arises whether the epithelium of the villi, as well as of the glands, takes part in the secretion, and from the observations that have been made it must be answered in the affirmative, at least so far as the erepsin and the enterokinase are concerned.

But the principal function of the epithelium of the villi is to absorb. Water may be absorbed throughout the entire intestine, and the same is true of dissolved carbohydrates; both enter the blood capillaries through the intestinal epithelium. Concerning the absorption of albuminoids decomposed by the action of the gastric and intestinal juices, we know only that their products of decomposition enter directly into the blood. Whether, as often claimed, the intestinal leucocytes play an essential part is not yet positively proven. We are best informed concerning the absorption of fat, which is easily demonstrable with the microscope. The fat of the food is completely decomposed in the intestine, and the fatty acids thus set free are rendered soluble by the bile, and in this form they are taken up by the epithelium of the villi through the rod band. Within the cells the fatty acids are again combined into neutral fats and in this form the fat is conducted through the body of the villus in the central chyle space, and from there into the lacteals. The muscles of the villi play a part in its transportation that is not to be underestimated; when they contract the villus must become shorter, the body and with it the central chyle space must be compressed, and the contents of the latter be emptied into the lacteal, in which the valves which appear in the submucous plexus prevent a reflux.

The Liver

The liver originates, like all intestinal glands, as a protrusion of the entodermal intestinal tube, and is demonstrable in embryos 2 and 3 mm long as a diverticulum directed ventrally just beneath the spindle-shaped stomach. A lively proliferation of the epithelium now takes place in the ventral wall that takes the form of solid cell trabecula which unite into a network. While this trabecular formation constantly extends farther and farther in the ventral direction a cell mass grows out from the caudal wall of the primary liver sac,

the rudiment of the gall bladder. The primary liver sac increases in length, and we have in embryos 9 and 10 mm long a hollow duct leading out from the intestine, lined with several layers of cylindrical cells, the ductus choledochus, which splits into two solid cellular cords, the short, caudal one of which ends with a distinct, clublike thickening, the rudiment of the ductus cysticus, while the longer, cranial one divides repeatedly and passes over into the true liver, now evident as a considerable organ. At this time it consists of cellular trabeculæ joined together into networks, each composed of several cells in the section.

Even in its first stages the young rudiment of the liver is closely related to the omphalomesenteric blood vessel that grows into it. Twigs shoot out from this vessel between the trabeculæ and thus give rise to a system of blood spaces in the meshes formed by them. These completely fill the meshes and stick close to the epithelial trabeculæ. As brought out in the chapter on "Blood," the embryonal liver is intimately connected with the formation of blood. An enormous accumulation of primitive mesamœboids very soon appears in the diverticula of the hepatic blood spaces, which undergo great proliferation. These are the foci for the development of blood in the embryonal liver, and they disappear completely at the time of birth. We find in these foci erythrocytes in all stages of development, as well as numerous giant cells.

The trabeculæ of the liver are solid, without a lumen from the beginning. The lumen appears first in embryos about 10 mm long, and originates simultaneously in many places of the liver rudiment by the separation of the contact surfaces of the cells.

Gradually the lumina thus produced coalesce, and we thus obtain a system of anastomosing canaliculi that are lined with liver cells, and always have from three to five cells about the lumen. But this condition undergoes a change in the course of later embryonal life through the growth of the liver tubule, as we must now call it. A displacement of the cells takes place so that the lumen of the tubule is bordered by only two liver cells with their broad sides touching.

Simultaneously with the canalization of the trabeculæ of the liver the cystic and hepatic ducts and the gall bladder become hollowed out. In the former the cells simply separate, but in the gall bladder large vacuoles are formed which gradually blend, so that finally a cavity is formed, which is lined at first with several layers of epithelium, later with two, and finally with only one.

As is evident from this embryological study the liver is a compound branched tubular gland with many deviations from the general type, the most important of which are that its tubules unite to form a network, that neighboring tubules lie together, and that a lumen develops between their cells, so that a glandular cell does not belong to only one tubule, as in all other glands, but to several at the same time. (See Fig. 31.)

The liver has a **double function:** to produce its peculiar secretion, like every other gland, which is carried by the excretory ducts into the intestine, and to elaborate in its cells substances that pass directly into the blood and are carried by it to the organism. The secretion of the liver is the bile, a yellow brown, sticky, viscid fluid of intensely bitter taste and alkaline reaction.

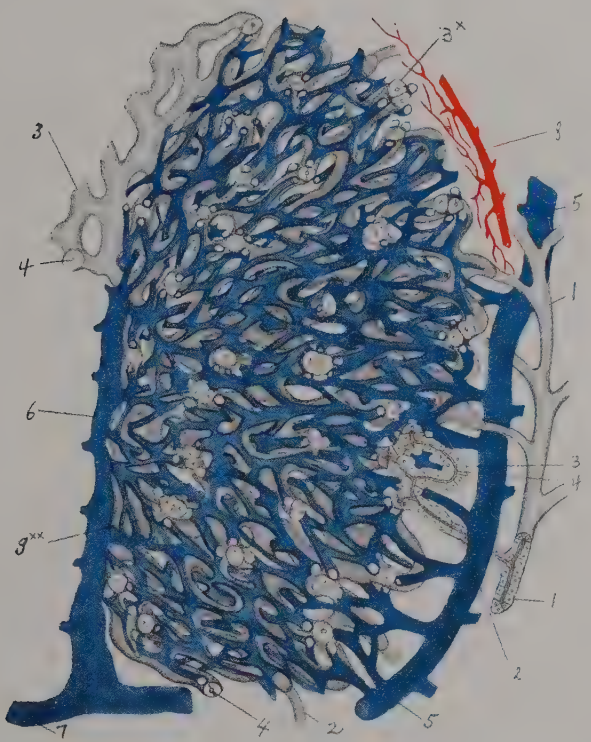


Fig. 31.—Structure of the Liver.

1, interlobular biliary duct; 2. intermediate piece; 3, liver cell trabecula, one of which divides at 3*, and two come together at 3** with the lumen of a biliary capillary between them; 4, biliary capillary; 5, interlobular vein sending its capillaries, that embrace the liver cell trabecula, into the lobules; 6, central vein, into which these capillaries assemble; 7, sublobular vein; 8, twig of the hepatic artery which branches in the interlobular connective tissue.

It contains considerable quantities of solid constituents, the most important of which are the ***biliary salts*** and the ***biliary pigments.*** The former are sodium salts soluble in water of two organic acids, glycocholic and taurocholic, which in turn are important products of the decomposition of the albumin of the food. The biliary pigments, **bilirubin** and **biliverdin,** are likewise the alkaline salts of two acids, and the latter is a product of the oxidation of the former. Both come from the blood and are derivatives of hæmoglobin. The chief use of the bile when emptied into the intestine is to dissolve fatty acids and to activate the fat-decomposing ferment of the pancreatic juice.

The products of the liver cells borne away by the blood are **glycogen** and **urea.** Glycogen is a polysaccharide and is doubtless a reserve substance formed preponderatingly in the liver, though also in other places, from the sugar brought by the blood, and perhaps also from fat and albumin, and stored away to be given up to the blood at the proper time. Urea, also one of the most important products of the decomposition of albumin, is formed not exclusively in the liver but in many other organs as well.

Like every other large gland of the digestive tract, the liver is surrounded by a capsule, **Glisson's capsule,** external to which lies the peritoneum over the greater part of its surface. Glisson's capsule consists of connective tissue containing a few elastic fibers, and sends septa into the parenchyma of the liver. It also enters the organ with the blood vessels and biliary passages at the porta of the liver, and finally divides the parenchyma into small prismatic areas 1 to 3 mm in diameter, which are called **hepatic lobules.** Although these lobules are quite distinctly visible macroscopically in consequence of the difference in the vascularity in their peripheries and centers, yet their delimitation by the connective tissue forming the interlobular septa is very imperfect, so much so that it is difficult to distinguish the lobules apart microscopically (Pl. 53, Fig. 128). Great numbers of fibers extend from the interlobular connective tissue into the lobules and surround the cellular trabeculæ with a close-meshed network that is difficult to demonstrate by ordinary histological methods, and can be made visible only by a special procedure. These interlobular fibers, which also occur in other glands, are known as the **lattice fibers.**

We will begin the description of the structure of the liver with the system of efferent ducts, taking the same course that we have followed in the consideration of other glands. The **hepatic duct,** the excretory duct of the liver, is lined with a simple, cylindrical epithelium full of goblet cells, next to which comes a connective tissue propria, with circular and longitudinal smooth muscular fibres outside of this. Entering the porta of the liver the duct divides first into coarse and then into finer branches, which run with the branches of the hepatic artery and portal vein in the connective tissue, and have the same structure as the hepatic duct except that the enveloping muscular fibers are absent and that the epithelium contains no goblet cells. The cylindrical cells present very distinct cement edges. The very minute **interlobular ducts** form wide-meshed plexuses about the blood vessels, from which numerous twigs extend to the periphery of the lobule and then turn toward the parenchyma, at the same time splitting up. This last part of the

excretory duct system, which may be called the **intermediate piece,** as in the salivary glands, has a very narrow lumen and is lined with low cuboidal cells (Pl. 54, Fig. 129). Following along we see how the much larger liver cells suddenly take the place of the cuboidal in the duct, and the intermediate piece is changed into the **liver cell trabecula,** or **liver tubule,** its lumen into the **biliary capillary.** While the lumen of the intermediate piece is surrounded by four or five epithelial cells, the biliary capillary is bounded by only two liver cells. The liver cell trabeculæ, which are the secretory tubules of the liver, pass through the lobules from the periphery to the axis, where they bend about and mingle with their neighbors. On the way they divide repeatedly, the branches anastomosing and forming radiating meshes in the lobule. The conditions then become very complicated, because neighboring trabeculæ lie together and a biliary capillary runs again in the middle of their touching surfaces, so that the same cell may be utilized in the wall of two or more biliary capillaries. In this the liver is unique and differs from all other glands, as in them each cell always appertains to only one secretory space. (See Fig. 31.)

The biliary capillaries thus form a network of minute canaliculi which passes through the entire hepatic lobule and lies within the liver cell trabeculæ. Their diameter scarcely exceeds 2 μ. Whether they have blind ends or, more correctly, blind beginnings, in man is hard to say.

The **liver cell,** the secretory cell of the hepatic tubules, has a polyhedral or prismatic form (Pl. 54, Fig. 130). It contains one, or very often two, spherical nuclei. Mitotic and amitotic figures are not infrequently met with in them. The cell body consists of a reticular or vacuolized protoplasm, the appearance of which varies a great deal according to the functional condition (Pl. 1, Fig. 1; Pl. 2, Fig. 7). After a full meal the cell body is occupied by coarse, irregular masses of a substance which is very slightly soluble in water, **glycogen,** while in hunger the glycogen is given up to the blood and the cell is full of little vacuoles that still contain minute granules of the substance. The cell also contains fat in larger or smaller drops, according to the state of the nutrition. The secretion of the liver cells, the **bile,** cannot be demonstrated in them under normal conditions, but in animals, and also in man under pathological conditions, indications have been found that the nucleus plays a great part in the secretion of the bile, with which the frequent occurrence of a double nucleus is in harmony. In such cases crystals of a substance resembling hæmoglobin have been found in the nucleus. The formation known as **Kupffer's vacuoles** probably serve to expel the bile from the cells. These are little, spherical vacuoles situated in the protoplasm of the cell near the biliary capillaries, which communicate with the latter through extremely minute tubules.

The liver is also distinguished from all other glands by the nature of its **blood supply,** which is double, as in the lungs, in that the entering blood stream is divided into a functional and a nutritive portion. The ***functional blood,*** i. e., that which carries to the liver cells the material for secretion, streams through the portal vein, while the hepatic artery conducts only the ***blood for the nutrition*** of the liver tissue. All of the blood is carried

away through the hepatic veins. The portal vein enters the substance of the liver at the porta in company with the hepatic artery and the hepatic duct. From its branches finally arise the interlobular veins, which run in the interlobular connective tissue enveloping each lobule with a dense vascular plexus. Numberless capillaries extend from this over the entire periphery of the lobule into its substance and form in it a close meshed vascular plexus that weaves about all sides of the liver cell trabeculæ, almost completely filling the meshes formed by these. It follows at once from the above description of the relations between the biliary capillaries and the liver cells that the biliary and blood capillaries never come in contact, but are always separated by the substance of the liver cells. Just as the liver cell trabeculæ radiate toward the axis of the lobule, so do the blood capillaries, which finally empty into the central vein occupying the axial space. That is, the central vein does not occupy the entire axial space, but, like the fruit stalk of a raspberry, it passes through only about two thirds of the entire length of the lobule, in order to receive from all sides the blood capillaries of the lobule. The central veins open into the sublobular veins, which run in the interlobular tissue, but are separated from the biliary ducts and the interlobular veins. The larger veins formed by their union likewise always remain isolated, and the hepatic veins finally open far from the porta into the inferior vena cava. The hepatic artery plays a very humble part as compared with the portal vein. It accompanies the latter closely in all its branching and ends with capillaries in the interlobular tissue, the blood from which is carried away in the sublobular veins (see Fig. 31) (Pl. 54, Fig. 130).

The **lymphatics** of the liver arise in unwalled spaces about the intralobular blood vessels. Although the existence of such spaces has been much contested of late, their presence is indicated by the fact that after ligation of the biliary duct the bile very soon appears in the thoracic duct. These unwalled intralobular spaces open on the surface of the lobules into the interlobular lymphatics, which either accompany the portal vein to the porta and empty into the hepatic glands, or wind about the veins of the liver and then, accompanying the vena cava, open into the anterior mediastinal glands. Besides these deep lymphatics, the liver has a system of superficial ones, some of which go to the glands just mentioned, others to the aortic, cardiac, superior pancreatic, and sternal glands.

The **nerves** of the liver come from the hepatic branches of the vagus and from the cœliac plexus. The great majority of them are nonmedullated. They enter with the vessels at the porta and accompany them in their course. In the interlobular connective tissue they form plexuses studded sparsely with nerve cells, from which twigs enter the lobules and twine about the cell trabeculæ. Knob-shaped endings on the liver cells have been described. It has not yet been established experimentally that the nervous system exerts an influence on the secretion of bile.

The Gall Bladder

The **gall bladder,** the development of which has already been explained, forms a muscular sac which receives the bile after it has been secreted in the

liver and gives it up to the intestine at the proper time. Its **mucous membrane** forms numerous folds and is lined by a single, high, cylindrical ***epithelium,*** the cells of which have a cuticular border on the free surface and contain numerous minute droplets that stain like mucus. These droplets leave the cells through minute canaliculi that pass through the cuticular border. It is questionable whether they are composed of a true mucin, or a nucleoalbumin. Next outward from the mucous membrane comes a connective tissue **propria,** richly provided with elastic fibers, and then a **muscularis,** consisting of a strong inner layer of circular muscles and a thin outer layer of longitudinal ones. The peritoneum covering the outer surface of the gall bladder is joined to the muscularis by a connective tissue subserosa.

The **nerves** of the gall bladder form a dense plexus of nonmedullated fibers between the two muscular coats that is furnished with many ganglia. It sends its fibers chiefly to the muscles.

The structure of the **ductus cysticus** and **choledochus** correspond in the main to that of the gall bladder, and differ only in the presence of glands, which may continue moreover on the neck of the latter. They are rather sparse in the cystic duct and attain their greatest development in the common bile duct, or choledochus. Their epithelial cells have the same structure as those of the gall bladder.

The Pancreas

The **pancreas** appears in the human embryo quite a short time after the development of the primary liver sac in the form of two diverticula, one on the cranial, the other on the caudal side of the hepatic protrusion. The former is the dorsal, the latter the ventral rudiment. Each is at first like the rudimentary liver, a rather compressed, saclike, lateral diverticulum of the intestinal wall, which in its further growth draws longitudinally into the mesogastrium and then communicates with the lumen of the intestine through a hollow pedicle. Finer twigs sprout out now from the gradually lengthening rudiment, which have at their ends clubbed thickenings that soon become hollow, the young alveoli. Through the rotation of the axis of the intestinal tube and the gradual elongation of the ductus choledochus, these two rudiments approximate, grow together, and finally become completely united in embryos about 20 mm long. The two efferent ducts from the primitive saclike rudiments form many anastomoses with each other, the dorsal usually undergoes involution, and the ventral becomes the main excretory duct of the gland. While the entire glandular parenchyma in embryos about 50 mm long consists of little spherical alveoli that are connected with the smaller excretory ducts by slender tubes, there subsequently appear in many places, and first in the youngest parts of the body of the gland, solid cellular sprouts, which may not become hollow even later, but lie in the parenchyma between the alveoli as independent, growing masses of cells constricted off from the epithelium of the duct. These are the formations known as Langerhans' islands, which later develop in all parts of the gland.

The pancreas is of the compound branched alveotubular type, and greatly resembles the serous salivary glands of the mouth in its plan of structure.

It differs in man from all other glands in the possession of masses of cells that are not canalized, **Langerhans' islands,** and of the **centroacinar cells** to be described later.

The **secretion** from the pancreas, the ***pancreatic juice,*** is a colorless, viscid, alkaline fluid that becomes gelatinous in the cold and is curdled by heat. It contains five ferments as characteristic constituents: ***amylopsin,*** which changes starch into sugar; ***steapsin,*** which decomposes fat; ***trypsin,*** which digests albuminous bodies; ***rennin,*** which coagulates milk; and a ferment that breaks up glucose. As was brought out in the discussion of the intestinal juice, trypsin is not contained as such in the pancreatic juice, but in a primordial form as protrypsin, which is changed into trypsin by the enterokinase of the intestinal juice.

The pancreas is exquisitely lobed. Its **connective tissue capsule** penetrates into the interior of the organ in the form of septa that subdivide the parenchyma into successive lobules ever becoming smaller, just as in the salivary glands. Numerous fibers of the kind described in the liver as lattice enter the lobules from the interlobular connective tissue and surround the alveoli with their plexuses.

The principal excretory duct of the pancreas, **Wirsung's duct,** is lined with a **mucous membrane** having a coat of **simple cylindrical epithelium.** Next to this is a connective tissue **propria** containing more or less numerous **mucous glands.** External to the propria is the **muscularis,** consisting of an inner, strong, circular coat, and an outer, longitudinal one that is developed only in places. At its beginning it lies in close relation to the ductus choledochus and opens with it on the plica longitudinalis duodeni. The duct is nowhere free, but is surrounded by glandular substance throughout its entire course. It receives many coarse, lateral branches, passes through the whole length of the gland, gradually becoming smaller, and ends in its terminal twigs in the cauda. The finer the ducts become the lower becomes the lining epithelium. The musculature disappears in the coarser branches.

From the most minute **interlobular ducts** branches pass into the lobules and become **intermediate pieces** on which the **end pieces** hang (Pl. 55, Fig. 132). Some of the latter are purely alveolar, some are rather elongated tubules. In no part of the excretory duct is there a secretory epithelium, such as we see in the salivary tubes of many of the glands of the mouth; the epithelium everywhere is indifferent.

In the salivary glands the conical secretory cells of the end piece directly adjoin the lower ones of the intermediate piece, but in the pancreas the conditions are somewhat different. The intermediate piece cells slip over the secretory ones so that we have both kinds in the end pieces, the conical or cuboidal secretory cells and the flat ones of the intermediate pieces directly bordering the lumen, which we know as **centroacinar cells** (Pl. 55, Fig. 132). The latter do not form a continuous coat, but lie apart, so that the lumen is directly bounded in many places by the secretory cells. The pancreas is the only gland in the human body that contains centroacinar cells.

The **secretory cell** of the end piece is conical or cuboidal, according to the form of the latter, and contains a roundish nucleus with nucleoli. The cell

body varies much in appearance with the functional condition of the gland. During hunger, when the cell is filled with secretion, a broad, dark **inner zone** distended with granules, and a narrow **outer zone** containing the nucleus, may be seen. These granules contain the abovementioned ferments of the pancreatic juice, or their preliminary stages, and lie in vacuoles of the protoplasm, which thicken toward the base of the inner zone about the nucleus. When the gland begins to secrete during digestion, particularly in consequence of the passage of the acid gastric juice from the stomach into the intestine, the cells evacuate their secretory granules, their inner zone becomes smaller, the denser protoplasm of the outer zone moves after it, and the nucleus migrates to the center of the cell. Fibrous differentiations of the protoplasm appear in the outer zone, similar to those found in the serous cells of the salivary glands of the mouth. We call these **basal filaments.** Their purpose is to reform the secretion; the filaments break it up into granules and these are transformed into secretion. The further the formation of secretion advances the larger the inner zone becomes again, so much the more these filaments are used up, and their remains may lie about the nucleus of the cell full of secretion in the form of a cap, the so-called **accessory nucleus.** Without doubt we have to do here with mitochondrial formations in these basal filaments.

Between the cells of the end pieces are numerous **secretory capillaries,** like those of the serous glands of the mouth, while the end pieces themselves are interwoven about by numerous fine fibers of connective tissue, similar to the lattice fibers of the hepatic lobules.

Langerhans' islands, already mentioned in the embryological introduction, form the second main constituent of the parenchyma of the pancreas. They form in the adult spherical or ovoid masses of cells placed in the interior of the lobules, and are therefore surrounded on all sides by the secretory end pieces and are fairly well delimited from them (Pl. 55, Fig. 131). Their average diameter is 150 μ, but this fluctuates like their number, which, according to modern researches, is between 170,000 and 200,000. They increase in number from the caput to the cauda and form at least 3% of the entire parenchyma of the gland.

The islands are wrapped about by fine connective tissue fibers, but so very imperfectly that they cannot be said to have a capsule. The parenchyma consists of roundish island cells with relatively large nuclei. The cell body is usually homogeneous and clear, the result of which is that the islands stand out in relief from the glandular parenchyma when properly stained (Pl. 55, Figs. 131, 132). Under certain circumstances fine granules are observed in the cells, and this has been interpreted as a sign that they have a secretory function. The cells form either a quite irregular mass, or one in which anastomosing cords can be perceived. The abundant supply of the islands with blood capillaries is striking.

The islands originate like the rest of the glandular epithelium from the epithelium of the young efferent duct, as brought out in the embryological introductory remarks, and the question arises whether they remain connected with the rest of the glandular epithelium or not. Views are divided in regard

to this. Some investigators take the stand that the islands are continuously connected with the secretory end pieces, that cells are constantly used up in the activity of the islands and replaced by transformation of end pieces into island cells, so that the proportion between the parenchyma of the gland and that of the islands remains undisturbed under normal conditions. Others, on the contrary, maintain that the tissue of the islands is absolutely free and independent.

With regard to the physiological properties of Langerhans' islands, pathological research has lately shown that they exhibit more or less serious changes in all cases of diabetes mellitus. From this, and from the results of experimental research, we must conclude that the island tissue is a ***gland with internal secretion.*** It provides a secretion that is given off directly into the blood vessels, and exerts a specific influence over the metabolism of sugar in the body. Hence, two secretory processes run parallel in the pancreas as in the liver, an outer and an inner; in the liver both issue from the same cells, in the pancreas from different ones.

The **arteries,** coming from the hepatic, splenic, and superior mesenteric, follow in general the course of the excretory duct, enter the lobules and form capillary baskets about the end pieces. The arteries of the islands first form a plexus about each, from which numerous tortuous capillaries pass through the island. The veins behave like the arteries. The vessels of the islands seem to have a certain independence of the others.

The **lymphatics** arise in spaces that sheathe the end pieces within the lobules of the gland, pass first between the lobules into vessels with walls, which twine about the blood vessels and empty into the pancreatico-duodenal, splenic, aortic, cardiac, and hepatic glands.

The **nerves** of the pancreas are for the most part sympathetic, and come from the hepatic, splenic, and superior mesenteric plexuses. They form an extensive plexus in the interlobular connective tissue, provided with very many ganglia, from which fibers enter the lobules and twine about the end pieces. Within the lobules we meet with large sympathetic cells having long processes. The nerves end between the cells of the end pieces. Many fibers also enter Langerhans' islands.

The Peritoneum

The entire peritoneum is covered by an **epithelium** which represents the most superficial layer of mesenchymatous cells of the former wall of the cœlom, and is composed of a single layer of large, low cells. Each cell has one flat, roundish nucleus, more rarely two, that bulges the free surface somewhat. The bodies of the adjoining cells are united by numerous protoplasmic bridges, so that the entire peritoneal epithelium forms a sort of **synctium,** in which the limits of the cell territories remain firmly fixed by the following arrangement. Each cell has on its free surface a homogeneous, structureless cuticular band; these bands are not confluent like the cell bodies, but are separated on all sides and luted together by a special cement. Thus a network of tortuous cement lines is formed in the superficial layer of the peri-

toneal epithelium which reduces silver salts and can easily be brought into view by treatment with them (Pl. 6, Fig. 20). In many places, though not everywhere, fine short hairs project from this cuticular band which usually are stuck together and must be regarded as a sort of brush band. Besides the **large celled epithelium,** there is a **small celled** one, but it is confined to the lower surface of the diaphragm, where it covers the places between the tendinous bundles. It differs from the other both in the smaller size of its cells and in having larger quantities of cement between the cell plates. These cells possess a certain contractility, so that the interstices between them, through which absorption takes place from the abdominal cavity into the lymphatics, may be enlarged. These heaps of cement were formerly described as stomata, but no open communication seems to exist between the abdominal cavity and the lymphatics.

The epithelial cells of the peritoneal cavity possess, as former mesenchymatous cells, a great ability to wander. They may break loose from their connections, become free in the abdominal cavity, and here develop ***phagocytic properties*** to a high degree. They may perhaps develop typical granulations in their bodies and become true granular leucocytes.

The peritoneal epithelium rests on a structureless, thin **basal membrane,** which is followed by the **propria** that consists of a superficial layer composed mainly of elastic fibers, and a deep one of connective tissue which blends with the loose connective tissue of the **subserosa.** The elastic fibers form true networks, while those of connective tissue interlace in all directions. The subserous connective tissue unites the parietal peritoneum with the subjacent abdominal musculature, the visceral peritoneum with the muscularis of the intestines, uterus, bladder, etc., and with the connective tissue coats of the glandular organs in the abdomen and pelvis.

The **mesentery** and omentum are simply duplicatures of the peritoneum in which the subserosa of both layers blends into a median lamella bearing the vessels and containing much fat. The fat cells cluster into masses that accompany the blood vessels over broad areas. We meet with many plasma, mast, and wandering cells in the connective tissue in addition to fibroblasts and fat cells. While the omentum is a perfect membrane, covered with epithelium on both sides, in the newborn the cellular coat gradually becomes imperfect in later life until finally apertures are formed here and there. In adults the omentum is cribriform in appearance; the beams between the apertures consist of connective tissue, and are incompletely clothed with epithelium.

The **vessels** of the peritoneum come from those that supply the abdominal organs and muscles, run for long distances in the subserosa, and form a vascular plexus in the propria. The **peritoneal nerves,** part of which are vasomotor, part sensory, have a like origin, and form plexuses in the subserosa and propria. Part of the medullated sensory fibers have free ends, part terminate in special end corpuscles of the Vater-Pacini type, which unite into groups, especially in the peritoneum of the anterior abdominal wall, situated just beneath the basal membrane. They come into account in the perception of the sensation of pain.

III. THE RESPIRATORY ORGANS

1. THE NASAL CAVITY

The nasal cavity in man has a double function, inasmuch as it is the olfactory organ, and also serves to warm, moisten and filter the entering current of air.

Embryologically it develops from two parts, one of which is the **paired olfactory fossa,** or **primary nasal cavity.** This is lined with stratified cylindrical epithelium and opens at its posterior end with the primitive posterior nares into the mouth, from which it is separated by the primitive palate. In this primary nasal cavity the turbinates develop, and also Jacobson's organ, which later undergoes involution. Then a substantial part of the mouth unites with the primitive nasal cavity to form the **definite nasal cavity** through the formation of the secondary palate joining the primitive posterior nares toward the cauda.

Conformably to the double function of the nasal cavity we find two areas of the lining **mucous membrane** that differ in structure, the **respiratory** and the **olfactory regions.** We will deal with the former alone at this place and defer the latter until we come to speak of the organs of sense. The olfactory region occupies only a very small part of the nasal mucous membrane, being confined to the superior turbinate and the corresponding part of the septum, while all the rest of the cavity belongs to the respiratory region.

The outer entrance of the nasal cavity is the **vestibule.** Here the skin of the alæ and of the upper lip passes into the nose and forms its lining. At first it retains completely the character of the skin, i.e., it is covered by a **stratified flat epithelium,** the most superficial cells of which are horny. The epithelium rests on a **connective tissue corium** that forms numerous **papillæ,** the height of which increases at first, after which they gradually spread out and disappear. The corium in the vestibule is richly provided with networks of elastic fibers and contains hairs, sweat glands, and sebaceous glands. These characteristic formations of the skin disappear about the middle of the vestibule, together with the horny layer, so that in the posterior and upper parts of the vestibule we have a stratified flat epithelium resting on a connective tissue propria, in which mixed, seromucous glands, similar in structure to those of the lip, take the place of the sweat glands.

The transition of the **skin** of the vestibule into the **respiratory mucous membrane** of the nose takes place in the lateral wall about at the limen nasi, on the septum in the region of the tubercle, on the floor still farther back, though these conditions vary in different persons. The transition is not so sudden as it is at the junction of the œsophagus and stomach, but the stratified flat epithelium gradually assumes the character of epithelium of the respiratory mucous membrane. That is to say, it becomes a ***stratiform ciliated cylindrical epithelium,*** the height of which ranges from 15 to 40 μ (Pl. 11, Fig. 35; Pl. 56, Fig. 133). The entire thickness of the epithelium is

passed through by the ciliated cell, which rests with a slender foot on the floor of the epithelium, and thickens gradually as it approaches the free surface. The intermediate spaces between their foot ends are filled with conical cells that rest with broad bases on the epithelial floor and taper upward, but never reach the free surface with their thin, finely attenuated points. Between the ciliated cells are many **goblet cells,** which like them descend to the floor of the epithelium. The ciliated cells present all the characteristics that have already been described; their cilia attain a length of about 6 μ and stroke toward the posterior nares. Distinct **cement edges** can be demonstrated between the upper ends of the ciliated and goblet cells.

The epithelium rests on a thin **basal membrane** that cannot be demonstrated in all parts of the nasal mucous membrane. Wherever it appears well developed it is cribriform, and processes of the connective tissue cells of the propria pass through the apertures it presents into the epithelium.

The propria of the nasal mucous membrane forms no papillæ and varies much in thickness, reaching its maximum on the interior turbinate. Its superficial parts consist of loose connective tissue, but the deeper we go the more abundant do we find networks of elastic fibers. **Numerous glands** are situated in the propria. First we find simple crypts, short diverticula of the epithelium into the propria which are lined substantially with goblet cells, but the mucous membrane also contains many branched alveotubular **nasal glands,** which resemble in their structure the glands of the lips and are therefore of a mixed nature. In addition to these, little **lymph follicles** are to be found in the propria.

The propria of the nasal mucous membrane is extremely rich in **blood vessels,** which mainly come from the ethmoidal and nasal arteries. The arteries in the deeper layers send their branches through the entire propria and break up into a capillary plexus beneath the epithelium and surrounding the glands. Thence the blood flows in a superficial venous plexus, and from this into a deeper one. These venous plexuses may assume the character of large masses of ***erectile tissue*** in certain parts of the nasal cavity in post-embryonal life, particularly on the inferior turbinate and on the medium surface of the middle turbinate. Here strong bundles of smooth muscle fibers, chiefly circular, are embedded in the venous walls, and this muscularity is surrounded by a connective tissue adventitia containing elastic fibers. By this means great masses of blood are accumulated in the mucous membrane of the turbinates for the purpose of warming the inspired air.

The **lymphatics** form a wide-meshed plexus in the mucous membrane of the respiratory part, collect into little trunks, part of which pass forward to the mandibular glands, part backward to the pharynx and to the deep cervical glands. The lymph passages of the nasal mucous membrane are connected with the arachnoidal space of the brain.

The **nerves** of the respiratory nasal mucous membrane come from the sphenopalatine ganglion, and are in part sensory fibers from the trigeminus, in part fibers from the sympathetic. They form a plexus in the propria and some of them end free between the epithelial cells of the mucous membrane, some of them in the musculature of the vessels.

The **mucous membrane of the accessory sinuses** resembles, on the whole, that of the nasal cavity, except that it is thinner throughout and contains fewer glands and no erectile tissue.

2. THE LARYNX

The lower respiratory passage appears first in embryos 2 to 3 mm long as a groovelike recess in the ventral wall of the epithelial intestinal tube just beneath the last pharyngeal pouch. This groove dilates at its caudal end into an unpaired rudiment of the lungs. The margins of the groove come closer and closer together from the sides until finally separation takes place and we have on the ventral side of the foregut a second epithelial tube that opens cranially into the pharyngeal cavity and has the rudimentary lung at its caudal end. Like the intestinal tube it consists of a double layer of epithelium, on the superficial cells of which cilia gradually appear. The cranial end of this respiratory tube, which subsequently grows considerably in length, forms with the adjoining parts of the pharyngeal rudiment the larynx. In embryos 7 to 8 mm long appear two sagittal elevations and one frontal across these, the arytenoid and epiglottic tubercles, the latter of which is directly contiguous to the rudiment of the tongue. In the mesenchyma about these epithelial rudiments a dense stratification of rounded mesenchymatous cells takes place in embryos 10 to 15 mm long, whence originate chondroblasts that produce cartilage. The advanced growth of the arytenoid tubercules leads to a median agglutination, so that now the pharynx communicates with the trachea only through a narrow transverse slit ventrally from the epiglottic rudiment. Caudally from this the epithelium puts out two lateral buds that are at first solid, but soon become hollow, connect with the lumen of the larynx, and form the ventriculum laryngis. The caudal one is marked by the absence of cilia on its epithelium and becomes the vocal cords, while the cranial portion furnishes the false vocal cords. The rudiment of the thyroid cartilage is paired; the two halves unite with another, unpaired, median rudiment into a single cartilage, which at first is in continuous connection with the great cornu of the hyoid bone, but this is severed about the end of the third month by the transformation of a piece of cartilage into connective tissue. The cricoid cartilage appears before the thyroid as a sort of tracheal ring. Simultaneously with the cartilages appear the rudiments of the laryngeal muscles, the striated fibers of which differentiate strongly in the elongated mesenchymatous cells. The glands of the laryngeal mucous membrane originate from the fourth embryonal month on as protrusions of the epithelium.

The larynx is lined by a **mucous membrane,** which is of a bright red color during life. The only exception to this is the covering of the vocal cords, which stand out distinctly because of their gray color. The mucous membrane has first an **epithelium** 50 to 60 μ thick, which has the same character as that of the respiratory part of the nose, i.e., it is a **stratiform ciliated epithelium** in which many **goblet cells** occur. But exceptions to this rule are furnished in various parts of the larynx. From above the **stratified flat epithelium** of the pharynx enters the opening of the larynx

and covers the entire oval surface of the epiglottis as well as a strip about 10 mm broad of its laryngeal surface. From this point the flat epithelium forms a marginal zone about the ***entrance to the larynx*** that varies a great deal in different individuals, and may send tonguelike strips in an irregular way into its interior. The **vocal cords** alone are quite constant in having their free edges projecting into the larynx covered with stratified flat epithelium. On the other hand, islands of respiratory epithelium are found on the oval surface of the epiglottis.

Taste buds occur in varying numbers in the epithelium of the laryngeal mucous membrane, but only in the stratified flat epithelium. They are most common on the laryngeal surface of the epiglottis and on the plicæ aryepiglotticæ. They are never met with on the vocal cords.

The epithelium rests everywhere on a homogeneous **basal membrane,** which is first developed in postembryonal life. Like that of the nasal mucous membrane it is full of fine pores.

The **propria** forms papillæ wherever stratified flat epithelium is present, except on the vocal cords, where ridges running lengthwise take their place. It is very firm and compact on the laryngeal surface of the epiglottis, on the vocal cords, and in the lower part of the larynx, less firm in the false vocal cords, and quite loose on the oral surface of the epiglottis, in the plicæ aryepiglotticæ, and on the posterior surface of the larynx. It is composed of connective tissue which forms very many networks and contains strongly developed ***elastic fibers,*** especially in its deeper layers. These form elastic membranes lying immediately upon the perichondrium and are thickened in places into bandlike masses, the most important of which have been named the **false** and the **true vocal cords.** The latter consists of a network of thick elastic fibers, the longitudinally running meshes of which are so narrow that the fibers run almost parallel. On this fibrous mass rests the epithelium, separated from it only by a thin layer of connective tissue and the basal membrane (Pl. 56, Fig. 134).

Lymph follicles appear in the propria in the region of the ventriculus laryngis. The propria is also the seat of the **laryngeal glands,** which penetrate more or less deeply into the cartilage in many places, especially on the epiglottis. They are absent only on the vocal cords, and are most numerous on the false vocal cords and in the mucous membrane of the ventricle, where their secretion serves to keep the vocal cords moist. In form and histological structure they resemble the glands of the respiratory nasal mucous membrane.

A connective tissue **submucosa** is developed only in the lower segments of the larynx; in the middle and upper portions the elastic tissue of the propria passes directly into the perichondrium, or the interfascicular connective tissue of the laryngeal muscles, which is likewise full of elastic fibers.

The **muscles** of the larynx are composed of bundles of striated fibers. In the vocal fold the longitudinal bundles of the vocal muscle and of the thyreoarytænoideus externus lie directly on the vocal cords.

The **cartilages** of the larynx are hyaline, with the exception of the epiglottis, the cartilagines corniculatæ and cuneiformis, and the vocal process of the arytenoid, which are elastic. They are enclosed by a perichondrium which is

rich in elastic fibers and frequently undergoes an asbestic change in the chemical constitution of its basic substance, the collagenous fibrils. Soon after puberty ossification of the cartilage takes place, earlier and more completely in males than in females.

The **arteries** of the laryngeal mucous membrane, which come from the laryngeal and thyroid, form a wide meshed plexus in the deepest layers of the propria, and then a closer one in the middle layers. From the latter minute twigs extend and break up into capillaries beneath the basal membrane and in the papillæ of the propria. They assemble into **veins** which accompany the arteries.

The **lymphatics** form a plexus in the upper, and another in the deeper layers of the mucous membrane, and are developed most abundantly in the ventricle, least so on the vocal cords. The vocal cords divide the lymphatics of the larynx into two independent districts, those of the upper flowing into the deep cervical glands, those of the lower into the prelaryngeal, pretracheal, and paratracheal.

Motor **nerves** supply the muscles of the larynx, sensory and vasomotor the mucous membrane. They come from the laryngeal nerves, with which run many sympathetic fibers, and form a plexus in the propria provided with little ganglia and isolated nerve cells. Part of the fibers coming from this plexus end free in terminal arborizations between the cells of the epithelium, while part form tufts in the connective tissue from which branched fibrillæ extend to end in terminal plates. They also twine about the glands and vessels.

3. THE TRACHEA AND THE EXTRAPULMONARY BRONCHI

The structure of the **mucous membrane** of the trachea and of the extrapulmonary bronchi deviates only in non-essentials from that of the respiratory mucous membrane of the nose (Pl. 57, Fig. 135). The **epithelium** is stratiform, ciliated, and cylindrical, increases only a little in height in the trachea, and contains many goblet cells. Islands of stratified flat epithelium are found in it and are particularly common in the pars membranacea tracheæ.

The **propria,** which is separated from the epithelium by an always distinct **basal membrane,** is very rich in **elastic fibers** that form a thick layer just beneath the latter, with the fibers running lengthwise and anastomosing freely. Many **lymphocytes** are met with between the elastic fibers. Under certain circumstances they may accumulate about the efferent ducts of the glands into follicular formations. A second elastic network lies beneath the propria, blends with the perichondrium on the cartilage, and elsewhere separates the propria from the submucosa.

The propria is abundantly supplied with large **glands,** exactly like the laryngeal glands in structure. They are most numerous in the interstices of the cartilage and in the pars membranacea.

A **submucosa** can be said to exist only in the membranous portion, where it consists of loose connective tissue with numerous elastic fibers, contains many fat cells, and joins the propria with the subjacent musculature.

The **musculature** consists of smooth muscle fibers that in their entirety form a band on the dorsal side of the membranous portion. The fibers run transversely and are inserted by means of short tendons into the free ends of the cartilaginous rings. By their contraction they draw the latter together and thus produce a not inconsiderable narrowing of the lumen of the trachea. To the dorsal side of these lie isolated bands of longitudinal fibers, part of which cross over to the musculature of the œsophagus.

The **cartilaginous rings** of the trachea and extrapulmonary bronchi are composed of hyaline cartilage and are covered by a perichondrium that is uncommonly rich in elastic fibers and is in continuous connection with the annular ligaments which join the ends of each imperfect ring. In later life an asbestic change and ossification appears in the cartilages of the trachea, but this comes later than in those of the larynx and is mainly confined to the upper half of the trachea.

The **arteries** for the upper half of the trachea come from the inferior thyroid, for its lower part from the internal mammary, and for the extrapulmonary bronchi from the aorta itself. They form little annular arches outside of the annular ligaments, which send branches to the mucous membrane, where they form an arterial plexus in the deeper layers of the propria. From this twigs are sent to the capillary plexus enveloping the glands and lying beneath the basal membrane. The course of the veins corresponds to that of the arteries.

The **lymphatics** form a very dense network in the propria, assemble into trunks that pass through the annular ligaments, and reach the paratracheal and deep cervical glands.

The **Nerves,** which come from the inferior laryngeal and directly from the vagus, and are associated with numerous sympathetic fibers from the pulmonary plexus, are quite similar in their behavior to those of the larynx. They form three plexuses in the propria of the mucous membrane, in which numerous ganglia are embedded.

4. THE LUNGS AND THE INTRAPULMONARY BRONCHI

In embryos 2 to 3 mm long the rudiment of the lung forms a little saclike dilatation at the caudal end of the just separated respiratory tube. This divides very soon into two branches, which in turn distend at their ends. Of these two principal bronchi the left divides into two, the right into three branches. The entire bronchial tree gradually develops by continuous dichotomous budding and increase in length, with terminal buds that are saclike and dilate into infundibula. Finally alveoli develop in the walls of the latter and of the respiratory bronchioles that lead to them.

The epithelial rudiment of the lung, which thus comes from the entoderm, is enclosed in its growth by a mass of mesenchyma that forms its outer covering. During the fourth month of pregnancy this proliferates strongly about the terminal branching and divides it off into little districts of parenchyma about 0.25 mm in diameter, the pulmonary lobules. In these constantly growing lobules the amount of connective tissue decreases as the branching of the epithe-

lial tube and the formation of alveoli increase. The individual lobules are defined very sharply from one another by the interlobular septa of connective tissue. After birth this interlobular tissue becomes greatly reduced, so that the boundary lines between the lobules become more and more effaced. The result of this is that several neighboring lobules blend, and the definitive pulmonary lobule is a conglomerate of several embryonal lobules.

The epithelium of the bronchi acquires cilia progressively from above downward, gradually becomes stratiform, and finally simple, ciliated cylindrical in the smallest bronchi. The young alveoli are lined with a single layer of cuboidal cells, and while the number of the latter constantly becomes greater their diameter remains about the same during the last months of embryonal life. At the time of birth a great distention takes place, while the cells thin out considerably and assume the character of respiratory epithelium. The mesenchymatous envelope of the bronchi likewise develops from above downward. First a propria develops in which successive glands appear. Cartilaginous nuclei originate in the bronchial wall and lead to the formation of cartilaginous plates down into the smallest bronchi. The elastic tissue appears relatively late and extends not only to the bronchi and bronchioles, but also to the walls of the terminal chambers and alveoles, which it surrounds with fine networks.

The function of the lungs is to remove from the venous blood, brought to it from the right side of the heart through the pulmonary artery, the carbonic acid that is constantly formed in all of the cells of the body by the process of combustion, and at the same time to load it with oxygen from the air for the purpose of further oxidation. Air that has been warmed and moistened in the upper respiratory passages is sucked into the alveoli by the inspiratory movements of the thorax and diaphragm, here gives up a part of its oxygen to the blood, receiving in exchange carbonic acid and water vapor, and is pressed out by expiration. The entrance of oxygen into the blood, and the passage of carbonic acid into the air, take place through the cells of the respiratory epithelium of the alveoli in accordance with the laws of absorption.

The lungs are constructed on the principle of the compound branched alveotubular glands. The **main bronchi** give off **lateral bronchi** that branch at first monopodically, later dichotomously, and gradually diminish in caliber. The bronchioles pass from the smallest bronchi each into a lobule where it splits up into the **intralobular bronchioles,** from which by further subdivision come the **respiratory bronchioles.** The **alveoli** in these are few, but in the terminal twigs they become much more numerous, so that finally they lie in contact with each other. These terminal twigs of the respiratory bronchioles, thickly studded with alveoli, we call the **alveolar passages.** The alveolar passage dilates at its end into the **infundibulum,** which is likewise studded with alveoli (Pl. 57, Fig. 136).

The lobulated structure of the lung is very evident on its surface. It appears to be divided into polygonal fields 5 to 10 mm in diameter, which are the bases of the conical, peripheral lobules. Toward the interior the lobules become irregularly polyhedral. They are separated by a scanty connective tissue connected with that accompanying the bronchi and the vessels. It continually diminishes after birth, as has been remarked already (Pl. 57, Fig. 136).

Like every other gland the lung, with its efferent ducts, the bronchi and bronchioli, is lined by a **mucous membrane,** which lies in many longitudinal folds in the bronchi. Its **epithelium** shows no noteworthy differences from that of the extrapulmonary bronchi, up to the entrance of the bronchiolus into the pulmonary lobule, but within these it increases in height and loses its basal cells, so that we have a simple ciliated cylindrical epithelium in which the goblet cells soon disappear. The cylindrical cells then gradually become lower and lose their cilia, so that in the respiratory bronchioles we have a low cuboidal epithelium, which gradually changes into the **respiratory epithelium** that lines the alveoli and also part of the respiratory bronchioles. This consists of large, extremely thin, irregularly bounded cells luted together by a cement. The nuclei all lie in the meshes of the network of blood capillaries, while the parts that lie on the capillaries themselves are without nuclei. The nucleated portion of the cell consists of a granular protoplasm, while the other part appears to be perfectly homogeneous.

The **basal membrane** beneath the epithelium of the bronchi becomes thinner and more delicate from above downward, and can scarcely be detected in the bronchioles.

The **propria** forms in the bronchi folds of the mucous membrane, in keeping with the longitudinal ridges, that consist essentially of elastic fibrous networks. Toward the outside these networks are sparser with loose connective tissue lying between them. The propria is pretty strongly infiltrated with lymphocytes. The deeper we go the thinner the propria becomes, but it always has fairly strong elastic fibers, and finally it passes over into the basal membrane of the alveoli. The basal membranes of adjoining alveoli blend and form the **alveolar septa.** This basal membrane is homogeneous, structureless, and has running in it numerous elastic fibers joined into networks, together with a few connective tissue fibers. The elastic fibers surround the alveoli like baskets, and form a circle about the base of each. The basal membrane also encompasses the blood capillaries accompanied by minute elastic fibers and is clothed on its inner side by the respiratory epithelium (Pl. 58, Fig. 137).

We see the **musculature** in the trachea as a continuous layer stretched between the ends of the imperfect cartilaginous rings. With the disintegration of the latter the muscular fibers advance farther inward and form a wickerwork in the propria, the meshes of which constantly grow larger as we go downward, but are maintained to the respiratory bronchioles, and sometimes circular fasciculi may be demonstrated in the alveolar passages outside of the structureless membrane.

The **glands** of the bronchi become steadily smaller and scarcer downward, but otherwise differ from the tracheal glands only in their relation to the musculature; their excretory ducts pass through the latter and their glandular bodies are placed outside of it between the fragments of cartilage. They disappear entirely in the walls of the intralobular bronchioles.

The cartilaginous rings of the larger bronchi become, through partial fusion, irregular plates, the processes of one projecting into the interstices of another, so that in the cross section the lumen of the bronchus is surrounded by several pieces of cartilage, partially overlapping or at a distance apart.

Then follows a progressive splitting up of these cartilaginous plates, which become constantly more scanty and finally disappear at the entrance of the bronchi into the lobules. Therefore the intralobular bronchi have neither glands nor cartilage in their walls.

The blood supply of the lungs is double, like that of the liver, the pulmonary artery taking the place of the portal vein, the bronchial arteries that of the hepatic. The pulmonary artery brings to the lungs the functional blood from the right side of the heart, i.e., venous blood which is to be arterialized in the alveoli of the lungs. Its branches accompany the bronchi and their branches, yet without coming into close relations, and finally enter the lobules with them. Here they weave a dense capillary network about the respiratory bronchioles and the pulmonary alveoli, embedded in the basal membrane of the latter. The arterialized blood is now gathered from this network into little veins that appear on the entire periphery of the lobules, unite into larger trunks, and then, following the course of the bronchi and of the pulmonary artery, unite to form the pulmonary vein. The bronchial arteries, on the contrary, bring arterial blood rich in oxygen to the tissues of the lungs directly from the aorta. They also follow the course of the bronchi, but continually send out twigs into the bronchial walls, supplying them and the surrounding connective tissue with blood. In the former they form two plexuses, one in the muscularis, and one beneath the epithelium. They do not enter the lobules, but run in the interlobular tissue to the surface of the lung, where they form another capillary plexus in the pleura. The bronchial veins follow a course quite similar to that of the arteries, but they do not carry away all of the nutritive blood of the lung, for part of the small veins empty into the pulmonary veins.

The **lymphatics** of the lungs are divided into the superficial and the deep. The superficial ones form a network over the surface of the entire lobe beneath the pleura, and the efferent vessels from this lead to the pulmonary hilum and thence to the bronchopulmonary glands. The deep lymphatics follow the course of the bronchi and blood vessels, and form a perilobular network about each lobule, but do not appear to enter them. They also empty into the pulmonary glands.

The **nerves** enter the lung from the pulmonary plexus and come partly from the vagus, partly from the sympathetic. They accompany the branches of the pulmonary artery and the bronchi and have many ganglia. In the propria of the bronchi they form a plexus from which fibers extend to the epithelium, the glands and the muscles, enter the lobules with the bronchioles and weave about the alveoli. Knoblike endings on the cells of the respiratory epithelium have also been described.

5. THE PLEURA

The visceral pleura, covering the surface of the lungs and penetrating deeply into its incisures, has essentially the same structure as the parietal which lines the thoracic cavity, and consists of a **loose connective tissue** in which are embedded many elastic fibers. It has no vessels and is covered next the pleural cavity by a simple **flat epithelium** quite like that of the peritoneum.

Between the epithelium and the connective tissue is a thin, structureless **basal membrane.** The pleura is joined to the subjacent tissues by a **subpleural connective tissue** in which lie the blood vessels and lymphatics. Its **nerves** come from various sources, the vagus, phrenic, sympathetic, and intercostals, and form a plexus provided with ganglion cells.

6. THE DIAPHRAGM

The rudiment of the diaphragm is composed not of one, but of several components, the transverse septum, mesentery, Wolffian folds, and body wall. At first it consists purely of connective tissue, but in the second embryonal month muscular fibers enter and soon appropriate it, so that in the third month the diaphragm is completely permeated by them. Later the muscular fibers undergo involution in the central part, leaving a central **tendinous part** surrounded by a **muscular part.**

The structures present in the **muscular part** are the ***pleura, musculature*** and ***peritoneum.*** Concerning the structure of the first and last nothing remains to be added to what has been said. The muscular fibers are striated and of a caliber varying in thickness from 5 μ to 20 μ. Segmentation may be observed very often in these fibers, just as with the muscular fibers of the tongue. Neighboring fibers anastomose and form networks.

In the **tendinous part** these ***muscular fibers*** become ***tendinous*** and are collected into bundles that take radiating or arched courses that are rather complicated. These tendinous fibers form two layers, one on the peritoneal, the other on the thoracic side, which contain strong ***elastic networks.*** In the center the two layers come pretty close together, but peripherally they are separated by connective tissue permeated by fat cells and interwoven with elastic networks. The peritoneum and pleura are the same as in the muscular part.

The **arteries** of the diaphragm come partly from the internal mammary, partly from the aorta, and form in the subserous and subpleural connective tissue large plexuses, from which twigs pass on the one hand to the muscle or tendon bundles, and weave capillary plexuses about them, on the other into the peritoneum or pleura and form subepithelial capillary plexuses. The **veins** follow the same course as the arteries and empty into the vena cava inferior.

The **lymphatics** form a subpleural and a subperitoneal plexus which have many connections and, like the blood vessels, send out twigs to weave networks about the tendon bundles and muscular fibers. The vessels assembled from these networks turn toward the pleura and run in numerous trunks to the sternal, and anterior and posterior mediastinal lymphatic glands.

The **innervation** of the diaphragm is supplied by the phrenic nerve, which is mainly composed of thick and thin medullated fibers, but also contains many that are nonmedullated. Within the diaphragm its branches form two plexuses, a subpleural and a subperitoneal, in which fibers from the solar plexus and from the vagus also occur. These two plexuses have many connections. Some of the fibers from the plexus supply the muscular fibers with motor end plates, others terminate in the connective tissue between the muscular and tendinous

bundles either free in antlered end formations, or in club-shaped end corpuscles. Finally a delicate end plexus is formed beneath the epithelium of the pleura and peritoneum.

7. THE THYROID GLAND

We will discuss the thyroid gland in connection with the digestive and respiratory organs, because it is related to them embryologically and originates from the entoderm of the upper part of the foregut. The first signs of the thyroid appear very early, in embryos 2 to 3 mm long, in the form of an epithelial cone that grows out of the ventral wall of the cavity of the mouth between the deep parts of the three primary rudiments of the tongue which have been mentioned. It lies at the upper end of the respiratory tube, which is splitting up at this time, and forms two lateral lobes that grow rapidly, while the pedicle joining it to the base of the tongue, the ductus thyreoglossus, becomes very slender and finally disappears, except for a blind sac at its cranial end, the foramen cæcum. This unpaired, median rudiment associates itself with a paired lateral proliferation of epithelium which comes on each side from the fifth pharyngeal pouch. The rudiment of the thyroid is quite solid at first, but begins to become hollow in embryos 6 mm long, and sends out shoots that are at first solid, later hollow, which become cut off by the surrounding connective tissue until they lie close together as little closed sacs lined with epithelium.

The thyroid is a ***closed gland,*** i.e., a gland with a cavity, but no excretory duct, and consists of numerous, densely packed **vesicles** lined with epithelium, the so-called **thyroid follicles.** These are commonly ovoid in shape, but may be elongated, and are studded with secondary protrusions (Pl. 40, Fig. 100). They scarcely exceed 0.1 mm in diameter and decrease in size with advancing age. The epithelium lining the follicles consists of a single layer of cells, the height of which varies. Usually they are about as tall as they are broad, but in some places they are cylindrical, in others quite flat. Each cell contains a spherical nucleus and a filamentous protoplasm in which mitochondria can be demonstrated. From the latter proceeds the formation of the secretion, which appears first in the form of minute, very acidophilic granules. As the secretion augments in the cell the granules blend and the entire cell body stains intensively. Such are called **colloid cells** to distinguish them from the former, which are known as **chief cells.** In addition we find in the zone adjoining the lumen minute granules of a fatty substance.

The secretion, the **colloid,** is emptied by the epithelial cells into the lumen of the follicle and fills it completely with a rather granular, very acidophilic substance. Its chief constituent is **thyroglobulin,** which may be decomposed by various agents into an albumin and iodothyrin. The ***content of iodine*** is characteristic of colloid. The contents of the vesicles also include the remains of cast off and broken down epithelial cells. The question how the colloid is emptied out of the closed vesicles is answered in various ways by different authors. The only thing certain is that it is to be found in the lymph passages about the follicles. Some think it gets here by osmosis, others think that it

passes through passages and clefts between the cells. Another theory is that the pressure of the ever increasing contents destroys the epithelium lining the follicle at a certain place, that the follicle then ruptures and allows the colloid to escape into the lymph spaces.

The colloid is carried by the lymphatics into the blood stream and is borne by it to the various organs of the body, where it has in some a stimulative, in others an inhibitive effect, according to the nature of a so-called hormon. When the secretion of the thyroid colloid is stopped, either by disease or by the extirpation of the organ, the result is arrest of growth, decrease of intelligence, hypoplasia of the genital organs, diminution of the amount of hæmoglobin in the blood, general emaciation, and finally death.

The thyroid is enclosed in a connective tissue **capsule,** which sends septa into the interior of the organ and divides it into lobes and lobules that become smaller and smaller, just as in the salivary glands. From the interlobular septa lattice fibers penetrate between the follicles and form basketlike capsules about them. No membrana propria has been demonstrated about the follicles.

The thyroid **arteries** are characterized by a relatively large caliber. They branch and anastomose freely in the interlobular tissue, enter the lobules and form about each follicle a large capillary basket placed just beneath the epithelium. The **veins** form several plexuses in the gland and conduct the blood into the thyroid veins.

The **lymphatics** likewise form networks about the follicles closely adjoining the epithelium. The above mentioned intercellular passages are supposed to open into these perifollicular networks. The lymphatics of the thyroid lead into the pretracheal, prelaryngeal, and deep cervical glands.

The **nerves** of the thyroid are for the most part sympathetic in nature and enter the gland with the blood vessels. They weave meshes about the follicles and end with little nodules on the epithelial cells. It has not yet been demonstrated with certainty that the nerves exert any influence over the secretion.

8. THE PARATHYROIDS

The parathyroids, or **parathyroid glands,** belong to the class of the so-called branchiogenous organs, i.e., they develop from the epithelium of the pharyngeal pouches and clefts. They originate in the third and fourth of the five pharyngeal pouches that develop in man, in epithelial thickenings directed dorsocranially. When the third and fourth pharyngeal pouches are cut off the parathyroids come into close relations to the thyroids, which are maintained thoughout life, and then appear as two little corpuscles lying in the furrow between the thyroid and the œsophagus, one at the upper, the other at the lower end of the lateral lobe of the thyroid.

Each parathyroid is enclosed in a connective tissue **capsule,** which sends into its interior septa that unite into a network. Within the meshes thus formed lies the **parenchyma,** in which the cells lie in reticulate ***columns,*** or in irregular ***heaps,*** or are grouped to form true **follicles,** each with a lumen. The last constantly grow more frequent with advancing age and differ in noth-

ing from the follicles of the thyroid. Two different forms of cells may be recognized as composing the epithelial columns and heaps, the **chief cells** and the **oxyphilic cells.** The former are usually the smaller and contain in their bodies larger masses of glycogen, the latter contain fine, oxyphilic granulations together with particles of fat. The follicles secrete colloid, which is also found in the peripheral parts of the corpuscle, frequently in clefts between the cells. The colloid of the parathyroid appears to contain less iodine than that of the thyroid.

The removal of the parathyroids leads to an increased muscular excitability, to the production of muscular spasms that are associated with serious trophic lesions in various organs.

The parathyroids are very richly supplied with **blood vessels.** The capillaries weave plexuses about the heaps and trabecula of cells, and have the character of sinusoids.

The **nerves** are similar to those of the thyroid.

9. THE THYMUS

The thymus also is a branchiogenous organ. It originates from epithelial thickenings that first extend in a ventral direction from the blind ends of the third and fourth pharyngeal pouches in embryos 5 to 6 mm long, and therefore is considerably later in development than the thyroid. The upper of the two rudiments grows toward the cauda, cuts itself off from the pharyngeal epithelium, and unites with its mate on the opposite side of the median line into an unpaired organ in which the paired rudiment can be recognized only in its cranial portion. The rudiment from the fourth pharyngeal pouch either undergoes involution, or develops into an accessory thymus. The thymus consists at first of densely packed epithelial cells. In embryos 50 to 60 mm long a loosening takes place in the mass of cells, which become stellate and anastomose. In the center of the lobules now formed by the entrance of connective tissue, the reticulum thus created is denser than in the periphery, and the cells are also larger, so that a medullary and a cortical substance can be distinguished. Then begins the most important stage in the histogenesis of the thymus; lymphocytes wander into the reticulum from outside and transform the *originally epithelial rudiment into a lymphoid organ.*

In its highest development, i.e., at the time of puberty, the structure of the organ is as follows: Each of the two lobes has a thin connective tissue **capsule,** which enters into the organ and divides it into secondary lobules about 10 mm in diameter, and these into smaller primary lobules (Pl. 39, Fig. 98). In other glands the lobules are completely separated by the connective tissue, but this is not the case in the thymus, where the parenchyma of all of the lobules is continuously connected, the connective tissue on each lobule leaving a sort of hilus through which a pedicle of parenchyma passes and unites with its neighbors, so that the final result is a thick parenchymatous cord forming the axis of each lobe.

The **parenchyma of the thymus** consists of the **reticulum** and of the **thymus cells.** In each lobule a clear, neutral **medullary,** and a dark periph-

eral **cortical substance** may be recognized. We will turn first to the reticulum, which involves the whole lobule and naturally enters also into the parenchymatous cord. As has been stated already it is composed of stellate epithelial cells which are larger and richer in protoplasm in the medulla, smaller in the cortex. This reticulum resembles that of the lymphatic glands, although it is of entirely different origin, and the similarity is increased by the fact that fibers appear in the cells, enter the cell processes and behave quite like the intercellular fibers of reticulated tissue. In addition true collagenous fibers enter the parenchyma with the blood vessels, which naturally have nothing to do with the cells of the reticulum.

Within the reticulum lie the **thymus cells,** found in both the medulla and the cortex, but much more abundantly in the latter. The medulla also contains special structural elements, Hassall's corpuscles. The majority of the cells, the so-called **little thymus cells,** are lymphocytes that have wandered in and have suffered only immaterial changes in their structure. They multiply within the parenchyma of the thymus and wander out from it as in other lymphoid organs. **Eosinophile leucocytes** also occur with them. **Hassall's corpuscles,** which are to be observed first in embryos 60 to 70 mm long, originate from the medullary cells and are larger or smaller, ovoid or spherical cellular masses having a distinctly laminated structure (Pl. 40, Fig. 99). One cell is always placed like a dish about the other cells, so that the central ones are the oldest. As enlargement advances all of the signs of degeneration appear in the central cells, their nuclei become pycnotic and disorganized, while the cell bodies undergo hyaline degeneration. The blending of neighboring corpuscles finally create formations that are visible to the naked eye. They attain their greatest development coincidently with that of the entire organ. Many leucocytes are also to be found together with the epithelial cells.

The thymus increases in size with fair rapidity after birth and reaches the acme of its development with the onset of puberty. Then signs of involution appear. Involution proceeds rapidly at first, then more slowly, so that only traces of the parenchyma remain by the sixtieth year. Its first indication is a poverty of the parenchyma in lymphocytes, as the multiplication of the latter in the organ comes to a standstill. Then the cells of the reticulum break down here and there, and are replaced by an increase of the connective tissue containing many fat cells.

With regard to the **physiology** of the thymus, modern researches agree that the organ has relations to the general growth of the body and to the metabolism of lime. Animals from which the thymus has been removed exhibit a marked inhibition of growth and an insufficient calcification of newly formed bone substance. Changes take place in their bones that constitute the clinical picture known in man as rickets. The thymus also appears to exert a powerful influence over the development of the testicles and ovaries. Premature puberty appears in animals on which a thymodectomy has been performed. Removal of the thymus seems to result in a poverty in the blood of leucocytes, especially of the transition forms.

The **arteries** of the thymus come from the internal mammary, the innominate, and the inferior thyroid. Their branches run between the lobules into a

plexus about each lobule, from which capillaries pass through the cortex and medulla to assemble into **veins** that follow the course of the arteries.

The **lymphatics** form plexuses about each primary lobule from which twigs radiate through the cortical layer in order to form a second plexus on the surface of the medullary substance. The latter is in turn permeated by a network of lymphatic capillaries that weave about Hassall's corpuscles. The larger lymphatics accompany the blood vessels and empty into the anterior mediastinal and deep cervical glands. Whether lymphocytes leave the thymus by way of the lymphatics has not yet been determined with certainty.

Nerves from the vagus and sympathetic reach the thymus in company with the blood vessels, but they are very scanty and nothing of the particulars of their relations within the gland is yet known.

IV. THE URINARY ORGANS

1. THE KIDNEY

The conditions presented by the embryology of the kidney are more complicated than those found elsewhere, because transitory urinary organs appear during embryonal life, and then disappear to give place to the permanent ones. The development of the urinary organs starts from the **primitive segment columns,** those portions of the mesoderm that connect the articulated primitive segment with the nonarticulated remainder. Little canals develop toward the cranial end of the columns, in embryos 2 to 3 mm long, that constitute, when taken together, the **pronephros,** or head kidney. These open on the one hand into the cavity of the body, while on the other they unite to form a longitudinal, cellular cord which grows caudally, remains for a long time connected with the epidermis and opens into the cloaca. This is the **Wolffian duct.**

The **primitive segment columns** that lie to the caudal side of the pronephros coalesce and then break down, with the exception of the most caudal segment, into a number of roundish masses of cells lying one behind another, which become hollow, like so many vesicles. While the pronephros undergoes involution as far as the Wolffian duct, this row of vesicles develops into a long, voluminous organ, the **Wolffian body.** With regard to the special process of involution we shall only say that a canaliculus comes from each vesicle and is attached at one end to the Wolffian duct, while it terminates at the other in a vesicular enlargement, the glomerulus of the Wolffian body, which is invaginated like the finger of a glove by a twig from the aorta.

Neither the pronephros nor the Wolffian body produce any secretion. The latter persists for a long time, and begins to retrogress in its cranial and caudal portions in the third month of pregnancy, while its middle portion takes part in the formation of the genital organs, as we shall see later.

The development of the **definitive kidney** sets in only a little later than that of the Wolffian body, and proceeds from the most caudal part of the primitive segment columns not broken down into balls or vesicles, and from the caudal portion of the Wolffian duct. A hollow shoot proliferates from the latter toward the former, shoving before it the tissue that covers it like a cap on the cranial side. Thus we have in embryos 5 or 6 mm long a hollow duct running dorsocranially from the place of opening of the Wolffian duct into the cloaca, and pouched at its blind end, on which rests a mass of cells, the **metanephrogenous tissue.** The pouched end now grows, while the column connecting it with the Wolffian duct constantly becomes longer and trough-shaped, so that the metanephrogenous tissue comes to lie in the trough, which is now directed dorsally. The hollow connecting column develops into the **ureter,**

the trough into the **pelvis of the kidney** and the excretory part of the renal parenchyma, the metanephrogenous tissue into the secretory portion of the latter and the renal connective tissue. The development of the excretory part of the parenchyma takes place in such a way that one terminal and two central tubes grow out from the trough-shaped renal pelvis, ramify, and form the primary collecting tubes. Thereby the metanephrogenous tissue is split up at first into four, and then into as many complexes as there are twigs, i.e., each branch and each twig has a cap of this tissue on its blind end. Each cap divides into two layers, an outer, which gives rise to the connective tissue, and an inner which is transformed into an epithelial vesicle. Each vesicle changes into a tortuous tube having one end connected with the blind end of its collecting tube twig, and the other spread out like a spoon. Blood vessels arise in the hollow of the spoon that are connected with vessels entering here from the aorta, and become completely enveloped by the spoonlike end of the canaliculus, so that finally they are enclosed on all sides by a double layer of epithelium. The two layers of epithelium blend at the place where the vessels enter, while at the opposite pole of the corpuscle the canaliculi proceed out of the external layer. Thus we have, omitting the pelvis, to distinguish three parts of the renal parenchyma; the first is excretory, comprises the efferent and collecting tubes, and develops from the Wolffian duct; the second is secretory and comes from the metanephrogenous tissue; while the third, having the same origin, represents the end of the glandular portion, the Malpighian corpuscles. Hence, while in all other true glands the parenchyma develops through continuous proliferation or protrusion of the epithelium from ***one*** place, the mouth of the excretory duct, in the kidney the excretory and secretory segments of the duct system develop separately. We shall meet with a similar condition in the closely related sexual glands.

The human kidney is a compound branched tubular gland. The excretory duct of each, the **ureter,** is dilated at its attachment to the **pelvis of the kidney,** which is prolonged into two or more large cups, the **calices majores.** Each large calix divides again into two or three small ones, the **calices minores,** which embrace the **renal papillæ,** one or several blended together. Each of the seven to twenty papillæ has a circular furrow within which the epithelium of the calix blends with that coming from the papilla, the latter being again continuous with that of the **papillary ducts.** These papillary ducts open in widely varying numbers at the top of each papilla; the small ones presenting ten or twelve, the large, coalesced ones as many as a hundred openings. Very soon after their entrance into the medullary substance of the kidney these papillary ducts divide dichotomously into the third order of **collecting tubules,** these in like manner into the second order, from which the collecting tubules of the first order are given off as lateral twigs. The collecting tubules of the second order are the longest; they begin at the end of the inner third of the parenchyma of the kidney and give off their first terminal branches at the beginning of the outer third. Those of the first order branch at right or acute angles and pass over into **intermediate pieces** that run in two short zigzag courses. Each of these turns again toward the center and passes into **Henle's loop,** which may be divided into a distal and a proximal limb. The former

runs about parallel to the collecting tubes toward the hilum of the kidney, passing through a more or less large extent of renal medulla, suddenly bends about and becomes the proximal limb, which runs back close to and parallel with the distal to the renal cortex, where it passes into the **convoluted tubule,** in which the canaliculus forms several very tortuous loops lying close together, and finally ends in **Bowman's capsule,** which lies within the convolution.

FIG. 32.

The **urine,** excreted by this complicated apparatus, is a yellowish, neutral or slightly acid, aromatic fluid with an average specific gravity of 1,017. It contains about 4% of solid constituents, of which two thirds are organic. The principal organic substance is **urea,** which originates everywhere in the body, partly as the direct, partly as the indirect decomposition product of the metabolism of albumin, and is excreted only through the kidney. Another important one is **uric acid,** which is present in the urine in combination with alkalies and is produced by the recomposition of nucleinic acid. Of the other organic constituents **hippuric acid** is of interest to us, because we can say with certainty that it is formed within the kidney itself from glycocoll and benzoic acid. Common salt and phosphoric acid may be mentioned as among the inorganic constituents.

Although the most of, and the most important, constituents of the urine are brought to the kidney by the blood, yet this organ is not simply a filter, but it functionates the same as other glands. The excretion of most of the water and salt probably takes place in Bowman's capsule, that of the organic constituents in the cells of the convolution and in the distal limb of Henle's loop. Water is probably absorbed from the proximal limb of the latter on the contrary so as to inspissate the urine, while the collecting tubes and papillary ducts serve exclusively to conduct away the urine.

We shall now discuss the individual sections of this complicated system, beginning with the papillary ducts, and consider the calices and ureter later.

The **papillary ducts,** which open on the surface of the papilla in the area cribrosa, are very short, about 0.2 to 0.3 mm wide, and are lined by a single layer of high cylindrical cells. Each cell projects with a round top into

Fig. 32.—Renal Canaliculi (after *Peter*).

A, with long loop; *B*, with short loop. 1, papillary duct; 2, collecting tubule of the third order; 3, collecting tubule of the second order; 4, collecting tubule of the first order; 5, intermediate piece; 6, distal limb of Henle's loop; 7, proximal limb of Henle's loop; 8, radiating piece; 9, convoluted tubule; 10, Bowman's capsule.

the lumen and contains a spherical or ovoid central nucleus (Pl. 59, Fig. 141). The cell body appears very clear and bright about the nucleus, darker in the periphery where the protoplasm contains threadlike mitochondria. Just beneath the free surface is a double central body. The epithelium rests directly on the strongly developed connective tissue of the renal papilla, as there is no membrana propria. The individual papillary ducts are fairly far apart.

The **collecting tubules** are exactly the same in their histological structure as the papillary ducts, except that the epithelium constantly becomes lower as the caliber decreases, and that a distinct, structureless membrana propria gradually appears. Naturally they come closer together as they approach the cortex, so as to be separated only by a scanty amount of connective tissue (Pl. 59, Fig. 140). In the minutest tubules, which are about 15 or 20 μ in diameter, the epithelium is cuboidal and rests on a well-developed membrana propria. Each cell contains a double central body just beneath the free surface, that sends a fine thread to the nucleus and a little flagellum into the lumen of the canal.

The primary collecting tubule passes over into the **intermediate piece** in which the lining cells gradually become lower, and Haidenhain's rod structure becomes more and more perceptible at their bases. As regards the central bodies the cells resemble exactly those of the collecting tubules. The intermediate piece has two parts that are almost vertical to each other, as we have seen above (Fig. 32). They are often studded with pouches and continue into the distal limb of Henle's loop that radiates inward, is slightly tortuous at first and then becomes straight.

The **two limbs of Henle's loop,** the ***distal*** or ***ascending,*** and the ***proximal*** or ***descending,*** lie close together and parallel, but we have also to differentiate two sections of the loop that differ in caliber and in their epithelial lining, one ***dark, thick,*** and lined with cuboidal cells, the other ***bright, thin,*** and lined with quite flat cells (Pl. 59, Fig. 140). The transition from one to the other of these sections never takes place in man in the vertex of the loop, but in either the distal or the proximal limb. In the long loops, i.e., those in which Bowman's capsules are situated in the central part of the cortex, it occurs in the distal or ascending limb. While in the short ones, or those having their Bowman's capsules in the peripheral parts of the cortex, it takes place in the proximal or descending limb (see Fig. 32). In every case a more or less long transition piece follows the intermediate piece and then the thick, dark section of the loop; this occupies only about three fourths of the distal limb of the long loops and suddenly passes into the thin section, which bends about farther toward the papilla and returns toward the cortex as the proximal limb. In the short loops we have likewise first a transition piece, then the thick, dark section, which bends about the vertex of the loop into the proximal limb, in which the transition into the thin bright section takes place. The latter is quite short and very soon passes into the straight initial portion of the convoluted tubule.

The epithelium of the thick, dark section consists of cuboidal cells with irregular outlines. The cells have many crestlike processes that fit into each other so as to produce an extremely complicated picture. The cell body con-

tains Heidenhain's rods and is given a dark appearance by numerous granules. The relations of the central bodies are the same as in the intermediate piece. Toward the latter the cells gradually clear up, become lower, and assume the characteristics of the intermediate piece cells.

The clear, thin section of Henle's loop has a diameter only about half as great as that of the other. As the cells that line it are very flat the lumen seems relatively large, although its actual size is no greater. The lining cells are large, flat, and provided with numerous short processes, like many pigment cells. Here also the processes of one cell fit into the interstices of another. The cells surround the entire lumen, so that we usually find in cross section only one nucleus bulging into the canal. The protoplasm is very clear, slightly granular, and encloses a double central body with a short flagellum extending into the lumen.

The transition of the proximal limb of the loop into the **convoluted tubule** takes place rather suddenly with a considerable increase of caliber. First the so-called **end piece,** or **radiating piece,** of the convoluted tubule runs toward the cortex until it reaches the level of a Bowman's capsule, where it forms several coils, which lie in part farther out than the capsule, then turn toward the latter and pass into it with a necklike constriction (Pl. 59, Fig. 139). The entire length of the canal in the convolution averages 14 mm. At the transition from the loop into the end piece the cells increase considerably in height and lose at the same time their crestlike processes. The cell body is still clear at first, and the protoplasm only slightly granular, but the granules soon become denser, the cell body darker, Heidenhain's rods appear in the basal zone, and the bristle fringe on the surface of the cell. The convoluted tubules are from 35 to 45 μ thick and are lined with cuboidal cells of about the same height and breadth, which have irregular, sinuate outlines, like those of the dark section of the loop. The large spherical or ovoid nucleus lies in the center of the cell. The cell body has a cloudy, granular protoplasm, and exhibits Heidenhain's rods very distinctly in its basal part. The roundish tops of the cells, in which the protoplasm is clearer, protrude into the lumen. The free surface of the cell is covered by a bristle band, beneath which is a double central body. Between the nucleus and the bristle band is a double central body. Externally the canaliculi are bounded by a distinct, structureless membrana propria (Pl. 6, Fig. 21).

The last section of the renal system of canals is **Bowman's capsule,** into which the initial piece of the convoluted tubule passes with a necklike constriction. This may be compared to a double walled goblet, of which the initial piece of the convoluted tubule forms the stem and then swells out to form its outer or parietal wall. The parietal passes over into the inner, visceral wall at the mouth of the goblet, which is very small. The cavity of the goblet is completely filled by loops of vessels, the **glomerulus,** which cover the inner wall everywhere so densely as to form a sort of epithelium. The cleft-shaped secretory space, which opens into the convoluted tubule, lies between the visceral and the parietal layers of the capsule. The entire Bowman's capsule, together with the glomerulus contained within it, is known as the **Malpighian corpuscle** of the kidney (Pl. 59, Fig. 139). This corpuscle has a diameter of

120 to 130 μ, and is enveloped by a structureless membrana propria, which is a direct continuation of the membrane of the canaliculi. The cells of the initial piece of the convoluted tubule become lower at the neck, lose their bristle bands and rod striations, and are continuous with the quite flat cells of the parietal wall of the capsule. They are very large and their limits can be determined only with great difficulty. The ovoid nuclei protrude into the lumen. At the place where the blood vessels enter, i.e., about opposite the place of entrance of the urinary tubules, the parietal bends over into the visceral layer. The vascular loops of the glomerulus are covered by flat cells, the limits of which cannot be made out, as a synctium.

The water of the urine is filtered from the vascular loops of the glomerulus through the visceral layer of the capsule into the space between this and the parietal layer, and runs from this space into the convoluted tubules where the principal part of the solid constituents are excreted. Material changes take place in the cells of the convoluted tubules during this **secretory activity.** During rest the cells load themselves with secretory material and protrude with clear tops into the lumen so that the latter becomes narrow and stellate. The bristle band is indistinct, while Heidenhain's rods on the contrary are very distinct. When the cell throws out its secretion the bristle band becomes much more evident, the clear top is lost, and the lumen becomes larger and rounder. The rods break down into granules so that the cells have a more uniform granular appearance. Modern researches have shown that we must consider Heidenhain's rods to be mitochondrial formations through the breaking down of which secretion is provided.

It still remains for us to study the ***topographical relations*** of the ***individual segments*** of the renal tubule. We may distinguish macroscopically in the kidney a central **medulla,** and a peripheral **cortex,** the former of which is whitish, the latter of a rather brownish color. The medulla presents the **renal pyramids,** the bases of which merge in the cortex while their apices lie in the papillæ (Pl. 58, Fig. 138). Between the bases of the pyramids the cortex penetrates centrally for a certain distance in the form of the **renal columns,** that separate the pyramids. The portion of the latter between the columns, the **limiting layer of the medulla,** appears striated radially because here the cortex enters the medulla for a distance in the form of thin striæ. The same relations are present within the renal columns, so that the entire limiting layer is composed of radiating, alternate light and dark striæ. The light stripes are the irradiations of the medulla into the cortex and are called **medullary rays,** the dark ones come from the cortex and form the **renal labyrinth.** Large blood vessels run in the medullary rays to the cortex and bound the areas of the parenchyma known as **renal lobules.** Each lobule has the form of a cone with its base in the cortex, its apex projecting into the medulla, with a medullary ray forming its axis, but not reaching its base, and surrounded by a mantle of renal labyrinth.

If we study now the course of the system of canals in the kidney with reference to this arrangement of the longitudinal section, we find it to be as follows: The papillary ducts and collecting tubules together form the medulla itself. The collecting tubules of the second order enter the medullary rays and here

give off at an angle the collecting tubules of the first order, which enter either the renal labyrinth, or the cortex proper, and there change into intermediate pieces. The loops arising from the latter run again toward the center in the same medullary ray with the collecting tubes of the second order for a greater or less distance into the medulla, bend about and return in the same medullary ray to the labyrinth or the cortex, where they change into the convoluted tubules and finally end in the capsules. Thus the Malpighian corpuscles lie in the renal labyrinth and the cortex, yet in such a way that the outermost layer of the latter contains none. The convoluted tubules have the same position, but extend into the outermost layers of the cortex and form the chief constituent of the latter. Henle's loops run in the medullary rays and in the medulla, the intermediate pieces in the labyrinth and in the cortex. The collecting tubules of the first order enter the labyrinth and cortex from the medullary rays, those of the second lie first in the medullary rays and then enter the medulla, in which the remaining collecting tubes and the papillary ducts naturally are situated.

The **stroma of the kidney** is very poor in true, gelatin furnishing connective tissue, which is found only in company with the larger vessels. Between the canaliculi and about the capsule there is a dense meshwork of minute fibrils that are similar to the lattice fibers of the liver and are thought by many authors to consist of reticulated tissue. The network gradually increases in amount in the medulla and attains a fair degree of development in the papillæ about the papillary ducts (Pl. 59, Fig. 141). On the outer surface of the kidney it is continuous with the **renal capsule,** yet the connecting threads are so slender that the capsule can be separated from the parenchyma more easily than that of any other organ. The renal capsule is a very dense, firm membrane composed of bundles of connective tissue that cross and interlace in all directions.

The **arteries of the kidney,** coming from the renal, are two main trunks, a ventral and a dorsal, which divide repeatedly and advance their branches peripherally as the ***interlobar arteries*** between the pyramids parallel to the surface. At the border between the medulla and cortex they break up into the ***interlobular arteries,*** which run toward the surface of the kidney within the labyrinth, thus between the lobules, in slightly tortuous courses, then usually perforate the capsule and terminate in the fatty capsule. On the way the interlobular arteries give off numerous lateral branches, each of which enters a Malpighian corpuscle as a **vas afferens.** In the corpuscle it divides into three or four branches, each of which breaks up into capillaries, so that the **glomerulus** produced consists of the same number of lobes. The capillaries reunite in the same way into three or four little trunks and these into a **vas efferens,** which leaves the Malpighian corpuscle close to the vas afferens (Pl. 60, Fig. 143). The vas efferens has the same structure as the vas afferens, except that its lumen is rather smaller, and must be regarded as an artery, while the glomerulus is considered to be a ***wonderful arterial network.*** Very soon after its exit the vas efferens breaks down into true capillaries which form plexuses about all of the urinary tubules in the cortex and labyrinth. These capillaries then go secondarily to the tubules of the medullary rays

which the vasa efferentia do not directly enter. Moreover the vasa efferentia enter the glomeruli in the most central part of the renal labyrinth, as well as the medulla, where they form long capillary plexuses about the collecting tubules and Henle's loops. These vasa efferentia are also known as **arteriolæ rectæ spuriæ.** The rest of the medulla is supplied by the **arteriolæ rectæ veræ,** which are given off at right angles from the interlobular arteries, radiate into the medulla in long tufts, and form long capillary plexuses about the straight urinary tubules. Thus the medulla is supplied partly with blood that has passed through the glomeruli, partly with blood that has not.

The ***venous blood*** of the cortex flows part toward the capsule, part toward the medulla. The capillaries that weave about the canaliculi in the outer zone of the cortex assemble into little venous trunks that turn toward the surface of the kidney, the **venulæ rectæ corticales,** and empty at right angles into little veins running parallel to the surface, the **venæ stellatæ** (see Fig. 33). Inasmuch as all of these veins in a little district of the cortex run in a radiating manner toward the center of the district, and there unite, stellate figures are produced on the surface of the kidney, when the veins are artificially or naturally distended, that join together, the **stellulæ Verheynii.** An **interlobular vein** flows from the center of this venous star, follows the course of the interlobular artery and empties into an arciform vein. The **arciform veins** run along the margin of the medulla and form a venous plexus from which the **interlobar veins** lead away, taking the course of the interlobar arteries. The arciform veins also receive the **venæ corticales profundæ,** which conduct the venous blood from the capillaries about the tubules in the inner zone of the cortex, as well as the **venulæ rectæ,** which bring all of the venous blood of the medulla, with the exception of that from the apices of the papillæ, which flows away through the veins of the renal pelvis.

The **lymphatics** of the kidney form a system of enclosed tubes which generally follow and twine about the blood vessels. In the cortex the lymphatic capillaries weave about the urinary tubules, surround each Malpighian corpuscle with a delicate plexus, and enter the glomerulus with the vas afferens. The lymph escapes in two directions: one into the capsule, where there is an extensive lymphatic plexus that anastomoses with the lymphatics of the fatty capsule, the other along larger trunks that accompany the blood vessels to the hilum of the kidney and pass thence to the aortic glands.

The **nerves** of the kidney come from the sympathetic aortic plexus about the renal artery, which receives a branch from the minor splanchnic, and also contains fibers from the vagus. Then enter the parenchyma with the arteries, weaves about the urinary tubules of the medulla and cortex, and end with arborescent twigs between their epithelial cells. They also enter the Malpighian corpuscles and are distributed partly to the vascular loops, partly to the epithelial cells of Bowman's capsule. Part of the fibers that enter the kidney are vasomotor, part sensory, part secretory. Until quite recently it was supposed that the kidney had no true secretory nerves, but their presence has been demonstrated experimentally of late. They doubtless come from the vagus.

2. THE PELVIS OF THE KIDNEY AND THE URETER

The surface of the renal papillæ, large and small calices, pelvis, and ureter is covered by a so-called **transitional epithelium,** i.e., by a stratified epithelium the cells of which do not materially decrease in height and are irregular in shape. The most superficial layer is composed of the so-called cover cells, which are large, polygonal, and flat, send taglike processes between the deeper layers, stain more strongly than these, and have a band of condensed protoplasm on their free surfaces. The simple cylindrical epithelium of the papillary ducts directly adjoins it in the area cribrosa. The epithelium is rather thin on the papillæ, but increases in thickness considerably in the calices and pelvis, where it is composed of as many as ten layers of cells and has a maximum thickness of 70 μ.

The epithelium rests directly on the connective tissue **propria,** which is permeated by nets of elastic fibers. On the papillæ the propria is very thin and is continuous with the papillary stroma, later it assumes a considerable thickness and juts into the epithelium in the form of longitudinal and circular ridges. In the ureter it forms longitudinal folds covered with epithelium and projecting into the lumen (Pl. 60, Fig. 144). Delicate septa that anastomose with one another penetrate still farther from the ridges of propria in the calices and pelvis into the epithelium and reach the covering layer, imperfectly dividing the epithelium into roundish or polygonal districts. The mucous membrane contains no glands.

Externally to the propria lies the **muscularis,** which cannot be sharply differentiated from it. It consists of smooth muscle fibers, begins at the place of origin of the little calix as a circular muscular layer about the papilla, the **sphincter papillæ,** then forms an irregular plexus on the calices, and a second circular muscle at the mouth of the calix into the renal pelvis. It becomes stronger in the pelvis and forms a continuous circular muscular layer, outside of which lie irregular, longitudinal muscular bands. In the ureter it increases considerably and may be divided into three layers: a strong inner layer of separate longitudinal bundles, a thick circular layer, and some scattered longitudinal bundles outside of this (Pl. 60, Fig. 144). The nearer we approach the bladder the more powerful does the musculature become, until finally it almost completely displaces the connective tissue of the propria. Near the mouth of the ureter strong external longitudinal muscles appear, which, together with the connective tissue adventitia, form the **ureteral sheath.** Arriving at the wall of the bladder the ureteral musculature maintains its independence and ends in the propria.

Outside of the muscularis of the calices, pelvis and ureter there is a connective tissue **adventitia,** which attains its greatest magnitude in the lower part of the latter through the reinforcement of the muscle just described.

The **arteries** of the calix, pelvis, and upper part of the ureter come from the renal, those of the lower part of the ureter from the internal spermatic, median hemorrhoidal, and inferior vesical. The smaller branches run in the propria and develop on one side a subepithelial, on the other an intramuscular

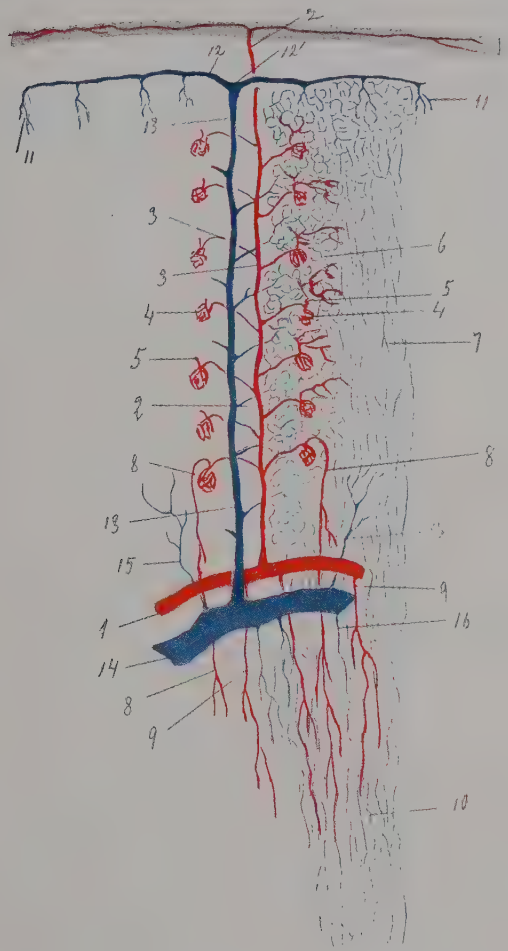


FIG. 33.—The Divisions of the Blood Vessels in the Human Kidney (schematic).

1, interlobar artery; 2, interlobular artery, the end piece of which, 2′, enters the capsule; 3, vas afferens; 4, glomerules; 5, vas efferens; 6, capillaries of the convoluted urinary canaliculi; 7, capillaries of the medullary rays; 8, arteriola recta spuria; 9, arteriola recta vera; 10, capillaries of the medullary substance; 11, venula recta corticalis; 12, venæ stellatæ that unite 12′ to form a stellula Verhezini; 13, vena interlobularis; 14, vena arciformis; 15, vena corticalis profunda; 16, venula recta.

capillary plexus. Capillaries from the former frequently enter the epithelium with the connective tissue septa and project in it like buds. The **veins** form a plexus in the propria and another in the adventitia.

The **lymphatics** form plexuses in the propria and muscularis, and empty into the aortic and hypogastric glands.

The **nerves** of the renal pelvis and of the upper part of the ureter come from the renal plexus, those of the lower half of the ureter from the spermatic and hypogastric plexus. They form a plexus in the adventitia and another in the muscularis, both provided with ganglia. Twigs from the muscular plexus enter the mucous membrane, but nothing is known in regard to their endings.

3. THE URINARY BLADDER

The **bladder** originates in the fifth week of embryonal life from the blind end of the intestinal tube, the **entodermal cloaca,** through the growing out of the **septum urorectale** from the lateral walls of the latter. It divides the entodermal cloaca into a posterior segment communicating with the intestine, the rectum, and an anterior, including the urachus and connected with the Wolffian duct, the **sinus urogenitalis.** The latter breaks externally into the urogenital fossa in embryos about 16 mm long. After the ureters have grown out from the Wolffian ducts the common opening of the two widens into the urogenital sinus, which grows constantly in length, takes up this dilated portion, and removes the opening of the ureter cranially from that of the Wolffian duct, which now turns again to the cauda. The segment of the urogenital sinus lying between the two contracts at the beginning of the third embryonal month, and thus separates the cranial portion with the urachus and the openings of the ureters to form the bladder. The epithelium of the bladder therefore has a double origin: part of it comes from the entodermal terminal portion of the intestine, part from the mesodermal epithelium of the Wolffian ducts and the ureters. It is flat before the growing out of the septum urorectale in the region of the ventral wall of the cloaca, later becomes cylindrical after separation from the rectum, and then becomes stratified in two or three layers. The surrounding mesenchyma condenses, the cells elongate, and smooth muscular fibrils begin to develop in embryos 20 to 25 mm long.

The structure of the bladder, which serves as a collecting reservoir for the urine flowing out of the ureters, conforms closely to that of the ureter. We may differentiate in its wall a mucous membrane, a submucosa, a muscularis, and an adventitia. In addition a large part of its outer surface is covered by peritoneum.

When the bladder is empty its **mucous membrane** lies in prominent folds, except at the trigonum, but when it is full they are quite low. The mucous membrane is covered by only from two to four layers of ***epithelium,*** the deepest layer of which is composed of cylindrical cells, while the most superficial resemble the covering epithelium of the renal pelvis (Pl. 11, Figs. 33 and 34). The form of the cells as well as the thickness of the epithelium depend to a high degree on the condition of the organ as regards fullness. When the bladder is full the epithelium is low and the cells are broad, but when it is empty

the cells become narrower and higher and overlap one another somewhat, so that a multistratous condition may be simulated.

The epithelium rests directly on the connective tissue **propria** and projects into it solid cones of cells, short ***crypts,*** and true branched ***glands.*** These are found almost wholly in the fundus of the bladder near the mouths of the ureters, and are lined with a single layer of cylindrical cells. The propria contains networks of elastic fibers that increase in strength toward the outside, and passes without a sharp line of demarcation into the **submucosa** together with an increase of the elastic tissue. Little **lymph follicles** may be found here.

The **muscularis** is composed of smooth muscle fibers and consists of three interlacing layers, an inner and an outer longitudinal, and a middle circular (Pl. 61, Fig. 145). The first is strongest over the fundus of the bladder, the circular muscles are well developed everywhere and form a muscular swelling about the opening of the urethra, the **sphincter vesicæ.** The outer muscular layer extends from the neck of the bladder chiefly over the anterior and posterior surfaces. Between the muscle bundles lies abundant connective tissue reinforced by networks of elastic fibers.

The outer surface of the muscularis is covered by a thin connective tissue **adventitia,** which blends posteriorly with the subserous tissue of the peritoneum and anteriorly with the connective tissue of the pelvis.

The **arteries** of the bladder come from the hypogastric and the median hemorrhoidal. Their twigs form first a perivesical plexus, from which branches penetrate the bladder wall and form a submucous plexus, and from this comes the capillary plexus of the mucous membrane and of the muscularis. The **veins** form a submucous, an intramuscular, and a perivesical plexus; from the last the blood passes into the great vesical plexus.

The **lymphatics** form one plexus in the propria and another in the muscularis. They lead to the vesical, hypogastric, and iliac glands.

The bladder contains both motor and sensory **nerve fibers.** Most of them come from the sympathetic hypogastric plexus, a minority from the spinal sacral plexus. Within the bladder wall they form plexuses richly studded with ganglia and single nerve cells, from which fibers extend to the muscles and the epithelium. Free arborescent terminations and end corpuscles of the Krause and Vater-Pacini type are also to be seen.

4. THE URETHRA

When the ureter has separated from the Wolffian duct and turned cranially with the bladder, that is now becoming roomy, the portion between it and the mouth of the Wolffian duct contracts, separates the bladder from the urogenital sinus and forms the **primary urethra,** the epithelium of which therefore has a double origin like that of the bladder. In the ventral part it comes from the **Wolffian duct** and is therefore mesodermal, while in the dorsal part it is that of the **cloaca** and consequently entodermal. The further development of the urethra differs in the two sexes and follows that of the sexual organs. In females the urogenital sinus attached to the primary urethra broadens greatly

in a sagittal direction and moves more and more toward the cauda, so that finally the primary urethra, which shows only a little longitudinal growth, comes to lie with its mouth at the cranial end. In males, on the contrary, a union takes place between the urethra, the urogenital sinus and the urogenital fossa along the lower side of the penis, which is of ectodermal origin. This groove is closed in by the growing forward of the genital folds and a tube is formed that leads from the bladder to the tip of the penis, the **male urethra,** which, as we shall see presently, serves also as the excretory duct for the male germinal glands, and therefore functionates as the duct for both the urinary and genital organs. The lining epithelium comes mainly from the entoderm, but there are portions that come from the mesoderm, and the terminal section is from the ectoderm. Rudiments of glands appear in the mucous membrane of the male urethra in the third embryonal month that appertain to the sexual apparatus and will be treated of under that subject, but there also appear, in both the male and the female urethra, little glands that are properly their own, diverticula of the epithelium.

a. The Male Urethra

The **mucous membrane** of the urethra lying in the penis lies in many ***longitudinal folds*** that are obliterated when the tube is dilated during the evacuation of the urine, and possesses a variable number of recesses that have been called ***lacunæ*** (Pl. 64, Fig. 151). We distinguish three parts of the male urethra: the prostatic, the membranous, and the cavernous, the first occupying about two tenths, the second one tenth, and the third seven tenths of its entire length.

The **epithelium** covering the mucous membrane varies in these different parts. It is a simple continuation of the vesical epithelium at the bladder end of the urethra, and is transitional over the entire prostatic portion. The innermost layer of cells gradually becomes higher, and this results in a stratified cylindrical epithelium in the membranous portion. Inwardly we have a row of high cylindrical cells, outwardly one to three layers of low cuboidal cells, and this forms the entire mucous membrane covering of the membranous and cavernous portions of the urethra. In many places, particularly in the lacunæ, the cuboidal cells are wanting, and we have a simple instead of a stratified cylindrical epithelium. Islands of stratified flat epithelium that vary in size may also be met with. The stratified cylindrical is replaced by a stratified flat epithelium at the outer end of the urethra, which lines the fossa navicularis and the external orifice and is continuous with that of the glans penis.

The epithelium rests directly on the **propria,** as there is no membrana propria. The propria consists of longitudinal and circular bundles of connective tissue and contains many cellular elements in its subepithelial parts. Lymphocytes also are to be seen and may accumulate into little follicles. The propria contains many elastic fibers, forms the longitudinal folds that have been mentioned as obliterated during the evacuation of the urine, and has many papillæ in the fossa navicularis.

The above mentioned diverticula of the mucous membrane, the **lacunæ,** enter the propria, which is also the seat of numerous **glands,** known as **Lit-**

tré's. These are of the branched alveotubular type, often open into the lacunæ, and usually extend into the submucosa (Pl. 64, Fig. 151). They are situated mainly in the upper and lateral, less often in the lower wall of the urethra, and are lined with cylindrical or high conical cells with vacuoles in their protoplasm containing very oxyphilic granules. Groups of such cells also appear in the floor of the lacunæ.

The **submucosa** merges without any distinct border line with the propria, and blends with the **muscularis,** which is developed only in the posterior half of the urethra. The musculature consists of bundles of smooth muscle fibers that form an inner, longitudinal, and an outer, circular coat.

The blood vessels and nerves of the male urethra will be described together with those of the penis.

b. The Female Urethra

The female urethra is only about 3 cm long, and its relations are much simpler than those of the male. It likewise has a **mucous membrane** lying in longitudinal **folds.** The epithelium presents variations that are not immaterial in different individuals. The transitional epithelium of the bladder always enters the urethra, but soon changes to a stratified flat variety that continues over the external orifice and the vestibule of the vagina. In other cases a stratified cylindrical epithelium like that of the greater part of the male urethra is interposed between the transitional and the stratified flat, but sooner or later it gives place to the latter.

The **propria** is of connective tissue abundantly supplied with elastic fibers, and always has numerous ***papillæ*** that project into the epithelium. As in males, it contains ***crypts of the mucous membrane*** and ***Littré's glands.*** Two large complexes of glands are formed in the anterior part of the urethral mucous membrane which empty through special excretory ducts, the ductus paraurethrales, into the vestibule of the vagina near the mouth of the urethra. Structurally they resemble the Littré's glands of the male.

The propria of the female urethra possesses a rich **venous plexus,** the walls of which have no muscular fibers, that as a whole forms an erectile tissue. The corresponding **arteries** lie considerably farther out. Numerous bundles of smooth **muscle fibers** run between the veins, part of them circular, part longitudinal, which unite externally to form a strong layer of longitudinal muscles. Still farther outward are circular bundles of striated fibers that form near the bladder a closed ring, later an incomplete one open below.

The propria of the female urethra also contains a very extensive **lymphatic plexus,** especially in its deeper layers, which is connected with the lymphatics of the fundus of the bladder.

The **nerves** come from the hypogastric plexus of the sympathetic, and from the pudendal. They form plexuses in the propria studded with little ganglia, and terminate partly free in the epithelium, partly on the muscle fibers, and partly in special end corpuscles.

5. THE SUPRARENAL CAPSULES

The only thing there is to justify a discussion of the suprarenal capsules in connection with the urinary organs is that they are related by derivation and topographically, for as regards function they have nothing in common.

The suprarenal capsules originate from two quite different rudiments, the **interrenal organ** and the **suprarenal,** or **adrenal organ.** The former appears in the fourth week of development in the form of budlike proliferations of the epithelium of the cœlom, which unites into a median cellular mass on each side of the cranial end of the Wolffian body. The suprarenal organ originates in the second embryonal month by a migration of cells from the rudiment of the sympathetic to the dorsal side of the preceding, that form little complexes within which the cells differentiate in two ways. Some become true **nerve cells** with numerous processes, the others remain without processes and elaborate within themselves a substance characterized by its reaction to the salts of chromic acid; in other words, become **chromaffin cells.** In the lower vertebrates the interrenal and the suprarenal organs remain separate throughout life, or are connected only superficially, but in the higher vertebrates and man the cells of the suprarenal organ enter the substance of the interrenal and become enveloped by it, so that we have an **epithelial cortex** of the suprarenal capsule derived from the epithelium of the cœlom, and a **medulla derived from the** nervous system, hence from the **ectoderm,** the latter remaining in constant connection with the sympathetic nervous system.

The suprarenal capsules may be grouped best with the parathyroids as regards structure and function. Like them, they are solid glands, with no openings between the cords and trabecula of their parenchyma, and naturally no excretory duct. The secretion is taken away by the blood.

The organ is covered by a thick **capsule** of connective tissue, containing many fat cells, that sends **septa** into the parenchyma. Both the capsule and the septa contain, in addition to bundles of connective tissue, many elastic fibers joined together into networks. Throughout the greater part of the cortex these connective tissue septa form tubes lying close together, that radiate and gradually grow smaller, to unite into networks in the neighborhood of the medulla. As soon as they arrive at the medulla the septa break up into numerous bundles of fibers that enter the substance and are there lost.

The glandular substance is interposed in this connective tissue stroma in the form of **solid cellular cords,** which vary in course and arrangement in different parts of the cortex, so that three zones may be distinguished within the latter, the **zonæ glomerulosa, fasciculata,** and **reticularis.** The cellular cords begin in the zona glomerulosa in the form of spherical balls, or bend about in short loops; then they take a radiating, slightly tortuous course in the zona fasciculata, which is by far the greatest of the three, to join and form a network within the less massive zona reticularis (Pl. 41, Fig. 101).

The cells that compose these cords exhibit essentially the same structural relations in all three zones. They are polyhedral and rather elongated in the zona glomerulosa. They lie closely together, so that from two to four cells

may be seen in a cross-section of a trabeculum, and are largest in the zone fasciculata. Each cell contains a spherical nucleus and a vacuolized cell body; the vacuoles are smallest in the zona reticularis, largest in the zona fasciculata. The vacuoles contain coarse granules of a fatlike **lipoid,** developed from mitochondria in the cell protoplasm. A reticular apparatus has also been demonstrated very recently in these cells. A brown pigment is to be found in addition to the lipoid in the cells of the zona reticularis.

The **medulla** is not always sharply defined from the cortex, like which it consists of ***cellular cords*** that unite to form a network, but the meshes are larger and the cords thicker than in the cortex. The cells also are considerably larger, are polyhedral, have nuclei that are usually eccentric, and hold very fine granules in the meshes of their vacuolized protoplasm. They contain what is called the **chromaffin substance,** because of its great affinity for the salts of chromic acid, by which it is stained intensely brown, but it retains this property only a few hours after death (Pl. 41, Fig. 101). This substance, known also as **adrenalin,** is probably attached to the granules in a fluid condition and is given up by them to the blood of the surrounding veins.

This adrenalin, which has also been produced synthetically since its constitution as a relative of pyrocatechin was discovered, ***acts*** quite specifically on the ***sympathetic nervous system*** and the organs innervated by it, as is clearly shown by the considerable increase of blood pressure that follows an injection of this substance. Animals from which the suprarenal capsules have been extirpated soon die with symptoms of general loss of strength. The blood of such animals proves to be very toxic, and the supposition is that it contains poisons which under normal conditions are rendered harmless by the suprarenal capsules. It seems probable from comparative experiments that this vital, antitoxic action proceeds from the cortex and a lipoid produced by it, so that we have to ascribe different functions to the two genetically different parts of the suprarenal capsule, the cortex and the medulla.

Some of the **arteries** of the suprarenal capsule come directly from the aorta, some from the inferior phrenic and the renal. They pass through the capsule into the cortex, where they follow the course of the connective tissue septa, weave their capillaries about the cellular cords, and form a wide-meshed capillary plexus in the zona reticularis. Wide sinusoids develop from this in the medulla that fill the retiform spaces and assemble into the central vein. Another set of arteries, the perforating, take a radiating course in the septa through the cortex into the medulla, and there break up into capillaries that twine about the cellular cords of the medulla and then open into the sinusoids.

The **lymphatics** form three plexuses that are connected—a subscapular, a cortical and a medullary. They run in the connective tissue septa, and send out fine lateral twigs which embrace the cells of the cortex and medulla with capillary plexuses. The outflow of the superficial vessels is through little trunks that perforate the capsule, while the lymphatics of the medulla leave the organ with the central vein at the hilum. Part of the lymphatics of the suprarenal capsule empty into the para-aortic glands, part into the posterior mediastinal.

The **nerves** of the suprarenal capsule arise from the cœliac ganglion and the phrenic and renal plexuses. The splanchnic must be considered to be its secretory nerve. Like the lymphatics, the nerves form a capsular, a cortical and a medullary plexus, the last of which is best developed. Numerous sympathetic ganglia, composed of large and small multipolar cells, are to be found within the medullary plexus. The fibers that branch from this plexus pass to the chromaffin cells and terminate on them with basketlike endings.

6. THE CAROTID GLAND

A little nodule situated at the bifurcation of the common carotid artery, and known as the carotid gland, is connected genetically with the adrenal system. It belongs to the group of paraganglia derived from the sympathetic nervous system, and has its analogues in the medullary substance of the suprarenal capsule, in Zuckerkandl's organ lying at the bifurcation of the abdominal aorta, and in other accumulations of chromaffin substance that we find scattered about in the sympathetic ganglia.

The carotid gland, which is also called the **paraganglion intercaroticum,** is an accumulation of polyhedral cells, a greater part of which correspond in their structure and in their microchemical reactions to the chromaffin cells of the medulla of the suprarenal capsule. Many vascular twigs and nerve fibers enter the nodule, which is enclosed in a connective tissue capsule, and typical sympathetic nerve cells may be demonstrated in it.

7. THE GLOMUS COCCYGEUM

The glomus coccygeum should be mentioned by way of appendix. This was formerly considered to be one of the paraganglia, but modern researches have shown that it has nothing to do with the adrenal system, and that it proceeds from a ***proliferation of the wall of the median sacral artery,*** in which the smooth muscle cells lose their typical appearance. The little corpuscle is abundantly supplied with vessels, which are covered as with a mantle by these proliferated media cells.

V. THE MALE SEXUAL ORGANS

1. THE TESTICLES

Both the testicle and the ovary, the male and female germinal glands, originate from the metamorphosis of a common ***undifferentiated sexual rudiment,*** which we shall describe briefly.

The ventral surface of the Wolffian body becomes covered by the epithelium of the cœlom at the end of the first month of pregnancy, when it has developed its essential parts, which projects into the abdominal cavity as a high cylindrical epithelium and forms a longitudinal **genital ridge.** Large, roundish cells appear very soon in its middle portion along with slender cylindrical ones that wander in from outside; these are the **germinal cells.** These cells, which may be recognized easily from their structure, have been traced backward in their development, and have been found to originate through segmentation of cells that separate themselves from the remaining somatic cells with the segmentation of the ovum, later emerge from various places in the embryonal body, and all migrate into the genital ridge. The middle portion of the genital ridge consequently increases considerably in thickness and becomes detached from the retrograding cranial and caudal portions as the **germinal epithelium.** A cellular mass exists in the mesenchyma between the germinal epithelium and the Wolffian body, which expands in the form of a network of cellular cords and is known as the **reteblast.** This probably arises also from the epithelium of the cœlom.

Coincidently with the development of the germinal epithelium a second canal, **Mueller's duct,** appears near the excretory duct of the Wolffian body through a groove-shaped depression and a later separation of the cœlom epithelium from the surface of the Wolffian body. Its development advances constantly from the cranial to the caudal end of the latter, so that it finally opens into the sinus urogenitalis together with the Wolffian duct.

While the germinal epithelium proliferates into the much thickened mesenchyma in the form of **germinal cords,** the rudiment detaches itself still more from the Wolffian body and forms the **undifferentiated genital rudiment,** composed of the germinal cords, the reteblast, and the middle part of the Wolffian body; the caudal and cranial portions of the last and of the genital ridge retrograde and become the bands of the germinal gland. The excretory ducts are the Wolffian and Mueller's, which lie close together caudally on the genital cord and open into the sinus urogenitalis, which at this time is beginning to separate from the cloaca.

The testicle develops from this undifferentiated germinal trunk by the germinal cords that separate the mesenchyma pushing to the surface, and the dissolution of their union with the germinal epithelium, which is reduced to a single layer of cells. We have then the free surfaces of the germinal trunks

covered by a simple cuboidal epithelium, beneath which the mesenchyma forms a strong layer, the so-called **albuginea;** this sends septa, the **septula testis,** inward to the surface of the Wolffian body, with the cellular **germinal cords** situated between them. The germinal cords grow longitudinally in the spaces between the septa, their sections toward the Wolffian body remaining straight and forming the **tubuli recti,** while their peripheral portions become very tortuous and give off likewise tortuous lateral sprouts. These are called the **tubuli contorti,** but they do not become open until shortly before birth.

The tubuli recti converge inward and then unite with the network of the reteblast, which becomes the **rete testis** after its canalization.

The efferent passages of the **epididymis** are now to be added to the parts of the parenchyma of the testicle that come from the epithelium of the cœlom. These originate from the **Wolffian body.** The epithelium of the capsule of the latter begins to proliferate in the region of the germinal trunk, and advances toward the rete testis to unite with it. While the glomeruli enclosed by the capsule of the Wolffian body pass away, the newly formed canals continue in its canaliculi and open as such into the **Wolffian duct,** which now becomes the **spermatic duct.**

The testicles maintain their high position until the third month, when they begin to sink, taking with them their blood vessels and their peritoneal covering, pass through the inguinal canal, and finally come to lie in a cutaneous pouch called the scrotum. The details of this change of position will not be discussed here.

The testicle is covered externally by a dense connective tissue capsule, the **tunica albuginea** (Pl. 61, Fig. 146). It consists of numerous lamellæ of connective tissue, one over another, that enclose richly developed elastic networks. This albuginea is thicker above and behind, and finally passes over into a powerful mass of connective tissue known as the **corpus Highmori,** or **mediastinum testis.** The albuginea is covered externally by the visceral layer of the **tunica vaginalis propria,** which is firmly adherent to it, is composed of a subserosa and an epithelium, like the peritoneum of which it is, in fact, a part, and is continuous above with the parietal layer, from which it is separated on its anterior, lower, and lateral surfaces by a fine interstice. The albuginea sends out numerous partitions from its inner surface, the **septula testis,** which converge toward the upper, posterior pole of the organ and there pass over into the mediastinum testis. The parenchyma of the testicle is divided by them into very many conical **lobules.** From the apex of each lobule comes a seminal duct, at first straight and known as the ***tubulus rectus,*** but peripherally cast into coils and called the ***tubulus contortus,*** which divides several times in succession, the individual branches again thrown into coils, and finally loops about the neighboring tubules, so that each lobule of the testicle is a dense convolution of tubules which gradually coalesce and empty into a tubulus rectus. The diameter of the tubule constantly decreases, from 200 to 20 μ. Although the tubulus rectus is quite short, the length of a tubulus contortus is estimated as between 70 and 80 cm.

Each **tubulus contortus** has a dense **sheath** consisting of several lamellæ of connective tissue with flat connective tissue cells and elastic fibers between

them. On the inner side of this sheath is the **epithelium,** which has two components. As we saw when studying the embryology, the germinal cords that form the matrix of the tubuli contorti are composed of two kinds of cells, the immigrated germinal, and those of the epithelium of the cœlom. The former now preponderate and lie in the child's testicle in several superimposed layers; we call these the **primitive spermatic cells,** or the **archispermatocytes.** They are roundish cells lying together rather loosely, each of which contains a nucleus and a distinct double **central body** surrounded by a thick, filamentous envelope, the **idiosome.** The cells from the epithelium of the cœlom give way before the primitive spermatic cells, and are to be seen here and there as narrow, long, cylindrical formations, each of which rests upon the envelope with a broad base enclosing a nucleus, and reaches up between the primitive spermatic cells to the lumen of the canal. These are called **foot cells,** or **Sertoli's cells.** The semen is produced by the primitive spermatic cells, the foot cells playing only a subordinate part (Pl. 62, Fig. 147).

The **formation of semen,** or **spermatogenesis,** begins in man from the fourteenth to the sixteenth year, and continues without interruption, under normal conditions, until the onset of old age. Several successive stages may be recognized in the process, which is distributed uniformly over the entire length of each tubule in such a way that each successive segment is always found in a different stage from the preceding, so that the entire process may be followed in one tubule. The same is true of domesticated animals, but in wild animals a short period of semen formation, known as heat, is followed by a period of complete rest, during which the epithelium of the tubuli contorti assumes the characteristics of that of childhood.

We shall now review very briefly these stages of spermatogenesis (Pl. 62, Fig. 147). At the beginning of puberty mitotic segmentations appear in the primitive spermatic cells that lead to the formation of a new generation, called **spermatogonia,** or **spermatic mother cells.** They differ from the preceding only in being somewhat smaller and assemble into a continuous layer just beneath the membrane of the tubule. During the second stage a lively process of segmentation takes place in these spermatogonia. The daughter cells increase considerably in extent, form one or two rows situated more internally, and are known as **spermatocytes.** Each spermatocyte divides into two cells, the **prespermatids,** and each of these immediately divides again into two cells, the **spermatids,** so that four equivalent spermatids come from each spermatocyte. The prespermatids differ from their mother cells only in being smaller, but the still smaller spermatids differ from them in an important characteristic; they have only *half as many chromosomes,* because in the final segmentation the chromosomes do not split longitudinally, but twelve of the twenty-four in the mother star enter one, and the remaining twelve the other spermatid. This is called a **reducing segmentation,** and is found to play a similar part in the development of ova. Hence the number of chromosomes remains constant in fecundation, which consists of a fusing of the chromatin of the ovum and of the semen.

The young spermatids, each with only a half number of chromosomes, lie in several rows directly adjoining the lumen of the canal, and are transformed

into **spermatozoa.** In this process, to be described presently, the cells gradually become pointed and lie with their points in the central ends of Sertoli's cells, which about this time are provided with lobate processes and probably supply them with nutrition.

The individual tubuli contorti of the testicular lobules are separated by a sparse amount of connective tissue containing the vessels and nerves. We also find special cells in masses or cords, that are known as **Leydig's cells,** or the **intermediate cells of the testicle,** and together form the **interstitial gland** of the testicle (Pl. 62, Fig. 147). They are spherical, or made polygonal by pressure, 15 to 20 μ in diameter, with spherical nuclei and double central bodies. The protoplasm of the cell body is strongly vacuolized, with granules of a lipoid substance in the vacuoles, and acidophilic granulations and pigment granules in the protoplasm itself. These intermediate cells are of mesenchymatous origin and are developed more abundantly in the embryo than in the adult. Experimental researches, and still more the study of abnormal conditions, have made it probable that a substance is produced by these cells which enters the blood and causes the development in the body of the secondary characteristics of the male. Whether they also take part in the nutrition of the developing spermatozoa has not yet been determined with certainty.

The **tubuli recti** are, as we have seen, the short, straight ends of the tubuli contorti. They are lined with a simple cylindrical epithelium, which we have to consider to be a continuation of Sertoli's cells. At the transition of the straight seminal tubules into the **rete testis** the cells become quite low and the connective tissue wall is lost, so that the tubules composing the network look like clefts in the connective tissue of the mediastinum.

The **arteries** of the testicle come from the internal spermatic, enter the mediastinum, and break up here into branches that follow the course of the septula and send twigs into the lobules, the capillaries of which run in the interstitial tissue and weave about the tubuli contorti, but are always separated from their walls by connective tissue. The **veins** follow the course of the arteries and empty into the pampiniform plexus.

The **lymphatics** of the parenchyma of the testicle are imperfectly known, but they seem in general to follow the course of the blood vessels, and like them to form fine capillary plexuses in the interstitial tissue. They appear in the mediastinum and form a plexus in the spermatic cord, the efferent vessels of which lead to the paraaortic and preaortic lymphatic gland.

The **nerves** of the testicle come first from the spermatic plexus about the internal spermatic artery, and second from the deferential plexus about the vas deferens. By far the majority of them are nonmedullated fibers that follow the course of the vessels into the mediastinum and form plexuses in the septa and in the albuginea. They also enter the lobules and weave about the convoluted tubules, forming a plexus the terminal twigs of which penetrate into the deeper layers of the epithelium.

2. THE EXCRETORY PASSAGES OF THE TESTICLE

a. The Epididymis

The first segment of the excretory passage of the testicle is formed by the epididymis, which comes from the tubules of the Wolffian body, and is composed of the ductuli efferentes and the ductus epididymidis. The ductuli efferentes are encased by a striated **membrana propria** resting internally on the **epithelium.** It presents on its surface numerous pitlike depressions that do not bulge outward over the greater part of the membrana propria, but in rare cases lead into true branched glandular ducts (Pl. 62, Fig. 148). The epithelial cells are long and cylindrical between the pits, and decrease in height as they pass down to the floor of the pit, where they become low cylindrical, or cuboidal. Very distinct cement wedges are always to be found between the cell bodies. The nucleus lies in the center of the cell or near its free end. Numerous acidophilic and pigment granules are to be found in the vacuolized cell protoplasm. The free surfaces of many, but not of all the cells have tufts of cilia that stroke during life toward the ductus epididymidis. These have basal corpuscles, and a double central body beneath the ciliated margin. The secretory granules mentioned above also occur in these ciliated cells; when a cell is full of them the ciliated border is cast off and the secretion escapes, after which the cilia are replaced.

The structure of the **ductus epididymidis,** formed by the junction of the ductuli efferentes, is materially different. It likewise has a striated **membrana propria,** outside of which are several layers of circular, smooth muscle fibers (Pl. 62, Fig. 148). The **epithelium** has perfectly smooth surface and is much higher than in the ductuli efferentes. It is composed of two rows of cylindrical cells 40 to 50 μ long, with more spherical cells between their bases. Each cylindrical cell has a nucleus situated about in its center, and numerous secretory granules in its cell body. From its free end extends a tuft of threads 20 to 30 μ long, that stain intensively, but the only thing we know of their nature is that they are not cilia.

b. The Vas Deferens

The **mucous membrane** of the vas deferens lies at first in longitudinal folds, but farther down oblique folds appear between these, and finally quite a system of communicating folds is formed (Pl. 63, Fig. 149). It is lined with an **epithelium** that differs only a little from that of the ductus epididymidis. The cylindrical cells are still higher and gradually lose their granular contents. The pigment granules persist, multiply, and give the surface of the mucous membrane a brownish appearance. In the vicinity of the ampulla the tufts of threads projecting from the free surface of the cells pass away, and we have only a double row of pigmented epithelium, which may lose its basal cells and become simple cylindrical.

The epithelium rests upon a connective tissue **propria** that is separated from it by a striated **basal membrane.** The propria contains numerous elastic fibers and forms the basis of the folds. It passes over into a well

developed **submucosa** of connective tissue, that leads to the **muscularis.** The last is the most essential part of the wall of the vas deferens, which is over 1 mm thick and is composed of three layers of smooth muscle fibers, the outer and the inner longitudinal, the middle circular.

Externally the wall is covered by an **adventitia** composed of bundles of connective tissue and elastic fibers.

c. The Seminal Vesicles

The seminal vesicles have essentially the same structure as the vas deferens, of which they are simply diverticula. The tendency of the **mucous membrane** in the lower parts of the vas deferens to lie in anastomosing folds becomes much more marked and results in the formation of numerous larger and smaller fossæ, the walls of which are in turn covered with smaller anastomosing folds.

The **epithelium** is simple cylindrical, as in the ampulla of the vas deferens, and its cells contain, in addition to a finely granular brown pigment, many strongly acidophilic secretory granules.

The **propria, submucosa,** and **adventitia** are the same as in the vas deferens. The **musculature** has the same layers, but is on the whole more weakly developed.

The **arteries** of the seminal vesicles come from the inferior vesical and median hemorrhoidal, and form an intramuscular and a submucous plexus, as do also the **veins.** The latter also form an extensive plexus in the adventitia, which is connected with the neighboring venous plexuses.

The **lymphatics** are composed like the veins and flow into the hypogastric glands.

The **nerves** come from the hypogastric plexus and form a plexus studded with many ganglia in the adventitia, from which fibers extend to the musculature and the mucous membrane.

d. The Ejaculatory Ducts

The **mucous membrane** forms anastomosing folds also in the relatively short ejaculatory ducts. The **epithelium** is partly simple cylindrical on the tops of the folds, partly stratified cylindrical in the fossæ, and otherwise presents the characteristics of that of the vas deferens. In the vicinity of its mouth it gives place to the transitional epithelium of the prostatic portion of the urethra.

The **propria** does not differ materially from that of the vas deferens. The **muscularis** also is composed of the same three layers. At the entrance into the prostate the two outer layers are split apart by the veins that are strongly developed here, and the combination forms a sort of cavernous body.

e. The Prostate

The prostate appears in the third month of embryonal life, growing from the dorsal and ventral walls of the prostatic portion of the urethra in the form of solid and branching cellular cords that later become canalized. While the dorsal part retrogrades, the ventral rudiment proliferates into the sur-

rounding mesenchyma, which becomes differentiated into smooth muscle cells. Each cellular cord is a branched individual gland, and the whole of them, fifteen to thirty in number, later become united into a common glandular mass by the developing smooth muscular tissue. The muscle is not developed in females and the retrograde glandular tubes open as the ductus paraurethrales in the vestibule of the vagina.

In adults the prostate is a glandular mass of the form and size of a chestnut, through which pass the urethra and the ejaculatory ducts. It consists of a variable number, at least twenty, **separate branched alveolar glands;** the excretory ducts of some of these coalesce shortly before they empty, but the most of them remain open, each with its own duct, into the urethra on each side of the colliculus seminalis.

The **epithelium** of the excretory ducts is that of the prostatic portion of the urethra near their mouths, but this transitional variety gives place very soon to a ***simple cylindrical.*** The secretory cells of the alveoli are likewise covered with cylindrical epithelium (Pl. 63, Fig. 150). The height of the cell depends on the secretory conditions. The nucleus lies either at the base of the cell, or toward the center. The basal part of the protoplasm appears dense and contains mitochondria, its central part is vacuolized and contains in the vacuoles little drops of lecithin and granules of secretion that stain strongly. The latter are also to be met with in the lumen of the alveoli after they have been cast off by the cells. The lumen of the gland almost always contains spherical concrements that may have as great a diameter as 1 mm, and exhibit a concentric stratification. These **prostatic concretions** are produced by the deposit of layers from the secretion.

There seems to be no membrana propria. A **connective tissue** provided with numerous elastic fibers adjoins the epithelium on the outer side, and is permeated more or less by bundles of **smooth muscle fibers.** This musculature is so abundant in many cases as to cast even the glandular tissue into the shade, while in others it is more weakly developed. An involution takes place in old age, after the cessation of the sexual function, of the glandular substance and musculature at the cost of the proliferating connective tissue.

The prostate also contains the so-called **utriculus prostaticus.** This is a blind sac about 10 mm long, though in rare cases its length may be several centimeters, which lies embedded in the substance of the prostate and opens on the colliculus seminalis between the two ejaculatory ducts. It is originally lined with stratified flat epithelium, but later this is replaced by a ***stratified cylindrical epithelium.*** A scanty **muscularis** adjoins the connective tissue **propria** of the mucous membrane.

Embryologically this is a rudimentary masculine vagina, for it originates from the caudal end of the coalesced Mueller's ducts, which, as we shall soon learn, gives rise to the female vagina.

The **arteries** of the prostate, which are only moderately developed, come from the inferior vesical and the median hemorrhoidal, branch in the stroma, and form capillary plexuses about the glandular alveoli. The **veins** into which these assemble open into the vesico-prostatic plexus.

The **lymphatics** form a plexus about the alveoli that is connected with

another beneath the capsule. The efferent vessels lead from the latter to the iliac, hypogastric, vesical, and hemorrhoidal lymphatic glands.

The **nerves** of the prostate come from the hypogastric plexus, and contain both medullated and nonmedullated fibers. In the stroma they form a plexus studded with numerous ganglia, from which fibers extend to the muscles and to the glandular epithelium. The medullated fibers terminate in special encapsulated end corpuscles lying in the stroma and in the capsule.

f. Cowper's Glands

These are ***compound, branched, alveotubular glands,*** the alveoli of which communicate, situated in the trigonum urogenitale close to the bulbus corporis cavernosæ urethræ. The **excretory duct** of each gland, about 30 to 40 mm long and opening in the cavernous part of the urethra is lined by a **stratified cylindrical epithelium,** which may be simple **cuboidal** in the **branches.** These branches have many lacunal dilatations and lead either directly, or through the medium of further tertiary passages, into the **terminal chambers,** which anastomose together. The last are lined with a **simple epithelium,** the cells of which are dark and **cuboidal,** or clear and **cylindrical** according to the secretory condition. The nucleus lies in the basal part, the protoplasm is reticulate. Secretory capillaries lie between the cells, and a distinctly perceptible network is formed by the cement wedges. Whether these are mucous cells, as claimed by many, has not yet been determined with certainty.

The epithelium rests everywhere on a well developed **membrana propria.** Between the alveoli is a connective tissue **stroma** containing numerous elastic fibers and bundles of smooth and of striated **muscle fibers,** that forms a capsule about the gland, the muscular fibers of which join the musculature of the trigonum.

The **arteries** come from the bulbourethral. The **lymphatics** empty into the hypogastric glands. The **secretory nerve** is the pudendal.

g. The Semen

The **semen,** or **sperm,** is the milky, viscid, slightly alkaline fluid, with a peculiar odor, that is ejected from the ejaculatory ducts. The solid constituents amount to about 10%, and over 80% of these are of organic nature, chiefly nucleoproteids, albumin, albumose, and mucin. If semen is allowed to dry **sperm crystals** form in it which contain spermin as a base in combination with phosphoric acid. When potassic iodiodate is added to the sperm we obtain little dark brown crystals that resemble those of hæmatin; this is known as Floren's reaction.

Microscopically the semen contains ***spermatozoa*** as its principal constituent, together with cells more or less changed by death, coming from the excretory passages, wandering cells that have passed through the epithelium, and larger or smaller spherical concrements of the prostate.

The semen, the quantity of which may amount to 5 or 6 ccm at an ejaculation, is composed of the secretions from the testicle, the excretory passes, and the glands associated with the latter. The testicle furnishes the spermatozoa,

the epididymis a very albuminous secretion that serves as a medium for their nutrition and suspension. The seminal vesicles have a double physiological function: to serve as reservoirs for the semen, and to furnish a secretion to render the fluid thinner and so to favor the active movements of the spermatozoa. The secretion of the prostate, which is materially thinner than the semen, also reduces the consistency of the latter and probably furnishes the spermin. Little is known positively concerning the secretion of Cowper's glands, which is believed by many authors to be mucous.

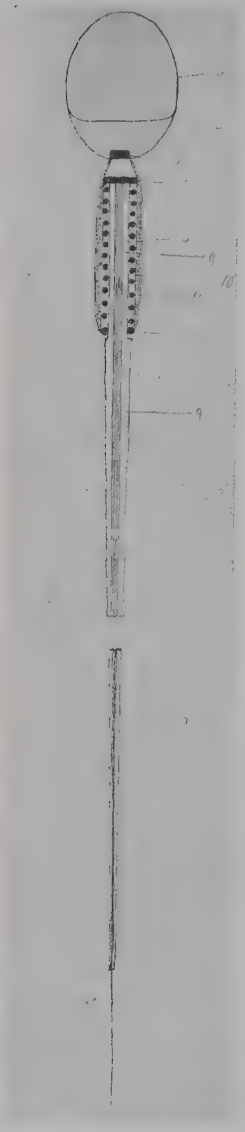


Fig. 34.

The **spermatozoa,** the most important constituent of the semen, remain to be described. The number present in an ejaculation varies a great deal, but may be given as 6000 to the cubic millimeter on the average. They are threadlike formations 50 to 60 μ long that maintain a *lively, serpentine movement* in the seminal fluid, in which they rotate about their longitudinal axes and are able to overcome a pretty strong resisting current. Their motility lasts for days in a test tube, is stimulated by dilute alkalies and neutral salts, and is inhibited by acids. The rapidity of the movements is given as 15 to 20 μ in a second under normal conditions.

Each spermatozoon is divided into a ***head,*** a ***connecting piece,*** and a ***tail.*** The **head** is about 4 or 5 μ long, 2 or 3 μ broad, and only 0.05 μ thick in the posterior section (Fig. 34). It has the form of an oval disc edged in front like a chisel. It is strongly refractive to light and has on its surface a line convex forward that separates a larger ***anterior part*** from a smaller ***posterior.*** The former is continuous with the chisel-like edge, that is also known as the **perforatorium,** with which the spermatozoon cuts into the ovum and enters into its substance. Special pointed and hooklike perforatoria are frequently found in animals. The staining reaction shows that the head consists mainly of chromatin, but no further structural details can be made out (Pl. 62, Fig. 147). The anterior part is covered by the **cephalic cap,** a special, thin, nonchromatic substance, because of which the posterior part always seems to stain more intensively with basic dyes than the anterior.

The **connecting piece** is a cylinder 5 or 6 μ long, having an oval cross section and an even diameter of about 1 μ. Its most anterior part, directly adjoining the head, is known as the neck. It contains **axis filaments,** consisting of fine longitudinal fibrils, which do not reach the head, but end at the peripheral part of the neck in several little nodules, the **anterior part of the posterior centrosome.** Similar nodules are situated at the junction of the neck and

Fig. 34.—Human Spermatozoon (after *Maves*).

1, head; 2, connecting piece; 3, tail; 4, anterior part of the head; 5, posterior part of the head; 6, axial thread; 7, anterior centrosome; 8, anterior part of the posterior centrosome; 9, involucrum; 10, spiral thread; 11, mitochondrial envelope; 12, posterior part of the posterior centrosome; 13, endpiece of the tail.

head, and form the **anterior centrosome.** The anterior centrosome and the anterior part of the posterior centrosome are united by a homogeneous intermediate piece, the **massa intermedia.** The axis filaments are covered in the region of the intermediate piece by an extremely thin, homogeneous membrane, the **involucrum,** which also extends over the tail. Then follows externally the contractile **spiral thread,** which rises in the anterior part of the posterior centrosome, wraps about the intermediate piece in close spirals, and is inserted into the circular **posterior part of the posterior centrosome.** The spiral thread is embedded in the homogeneous substantia intermedia, and is surrounded by the **mitochondrial sheath,** which contains the mitochondria and extends forward to the anterior centrosome.

The ***tail*** is subdivided into a ***main part*** and an ***end part.*** The former is 40 to 50 μ long and comprises about seven tenths of the entire length of the spermatozoon, while the end piece is of about the same length as the connecting piece. The entire length of the tail is passed through by **axis filaments** that gradually become more slender and are finally drawn out into a very fine point, and is covered by the **involucrum.** The latter presents a fairly marked thickening behind the posterior part of the posterior centrosome, tapers gradually with the axis filaments and ends with the main piece, leaving the fine, short end piece uncovered.

Aberrant forms of spermatozoa are not uncommon in human semen, such as those in which two connecting pieces and two tails extend from one normal head, the tails either completely separate or united posteriorly. Double headed spermatozoa also are comparatively common.

The *development of the spermatozoa* deserves a brief consideration. In the description of the epithelium of the convoluted tubules of the testicle we learned that the **spermatids** are their formative cells. These are spherical, with rather eccentrically placed nuclei and double central bodies just beneath the surface. During the metamorphosis the spermatids mass in the central ends of Sertoli's cells and maintain this position throughout the entire process (Pl. 62, Fig. 147). First the **nucleus** takes a more eccentric position and moves entirely into the end of the cell directed toward the wall of the tubule. It loses its spherical shape and becomes ovoid, its chromatin becoming condensed at the same time and finally formed into a homogeneous mass. Simultaneously the entire **cell** elongates, becoming at first ovoid and later conical. The apex of the cone is directed toward the wall of the tubule and is completely filled by the nucleus, while the base projects into the lumen of the canal. The two **central bodies** lie at first far from the nucleus at the periphery of the cell, one behind the other, so that we may distinguish them as a ***proximal*** and a ***distal*** with regard to the nucleus. A **fine thread** grows out of the latter, perforates the surface of the cell and protrudes free into the lumen of the canal. The proximal central body grows out into a transverse rod, and now both central bodies begin to move toward the nucleus. Having arrived, the posterior central body adheres to the posterior pole of the nucleus, while the distal lies farther back and sends its **caudal filaments** through the entire substance of the cell into the lumen of the canal. This distal central body now breaks up into a proximal head and a distal ring, the latter of which moves toward the posterior

pole of the cell along an axis filament. The young spermatozoon has therefore in this stage the shape of a truncated cone, the axis of which is two or three times as long as its base. Its anterior end is completely filled by the nucleus, which is now an oval disc. At its posterior pole is the proximal central body firmly attached to it, and at a little distance the proximal part of the distal central body, from which extend the axis filaments in the axis of the cell, passing through the distal ring-shaped portion of the distal central body at the distal pole of the cell, and out of the cell as a fine, long thread. Now the **mitochondria,** which have been distributed uniformly throughout the cell, assemble about the axis filaments, part of them forming the **spiral thread,** the rest lying about it as a **mitochondrial covering.** The remainder of the cell protoplasm breaks down and the axis filament becomes surrounded by an **involucrum** that probably originates through secretion. As soon as the metamorphosis of the spermatozoon is complete the latter leaves Sertoli's cell and enters the lumen of the tubule. It is still incapable of movement at first, and probably obtains its motility in the epididymis through the action of the secretion poured out there.

h. The Penis

The development of the external male genital organs proceeds quite like that of the internal ones from an ***undifferentiated stage,*** which we find in human embryos 20 to 30 mm long. On the ventral side of the anal depression lies the outer opening of the urogenital sinus, which runs along the ventral surface of the **genital eminence.** The latter runs caudalward in the roundish glans, its lateral surfaces formed by two folds of skin fused on the ventral surface, the **genital folds.** It is enclosed at its base by two likewise ventrally fused **genital prominences.**

The genital eminence now elongates in males and forms the **penis.** The **urogenital sinus** along its ventral surface is closed in by a caudally advancing adhesion of the urogenital folds, so that the urogenital tube, the **male urethra,** is enclosed in the ventral part of the penis and opens with its external orifice at the anterior end of the glans. The genital prominences grow ventrally at the root of the penis and unite in the middle line to form two little folds of skin united medially, the **scrotum,** into each of which a testicle descends later.

A circular line of epithelium proliferates from the posterior circumference of the glans backward and deeply into the tissue, so as to form a collarlike fold of skin about its base, the rudiment of the **prepuce.** The ring is incomplete ventrally, as at this time the urogenital sinus is still open in the region of the glans. When, after closure of the sinus, the prepuce grows forward to cover the glans it remains attached ventrally to the latter by a firm, bandlike connection known as the **frenulum.**

A thickening of the mesenchyma takes place at a very early time in the rudimentary penis, through which at first two cylindrical bodies originate that lie in apposition in the middle line and along the dorsal side of the urethra, the **corpora cavernosa penis.** The **corpus cavernosum glandis** develops in a similar manner in the glans at a later period, and the **corpus**

cavernosum urethræ about the urethra. Cleft-shaped hollow spaces then appear in these at first densely cellular bodies and communicate with each other. As the cells bordering them assume the characteristics of epithelium and the entire rudiment gains access to the venous system the bodies that were at first solid become erectile tissue. The mesenchymatous cells between the vascular spaces become transformed in great part into smooth muscle cells.

The penis is covered by a direct continuation of the **skin** of the neighboring parts. It has long hairs at the root of the penis, only short ones along its shaft. The deep layers of the epidermis contain pigment, the corium forms many high papillæ and is plentifully supplied with elastic fibrous networks that blend externally into a strong elastic stratum. The corium contains sebaceous and sweat glands. Anteriorly the skin is prolonged into a simple duplicature called the **prepuce** or **foreskin,** the ***outer layer*** of which is exactly the same as the skin of the penis, except that it contains no hairs, while the ***inner layer*** differs in having less cornification, a smaller amount of pigment, and no sebaceous or sweat glands. The inner layer passes over upon the glans in the **sulcus coronarius.** The epithelium at the external orifice is continuous with the stratified flat epithelium of the fossa navicularis.

Next internally to the skin is the **tunica dartos,** a layer of smooth muscular fibers, chiefly circular, which is connected with the layer of the same name in the scrotum and is lost anteriorly between the two layers of the foreskin. Then comes the **subcutaneous tissue,** a well developed connective tissue, poor in fat, in which run the vessels and nerves. This continues forward into the foreskin, where it unites the outer and inner layers. The strongly developed elastic fibers thicken internally into a powerful elastic stratum known as the **fascia penis.** The tendons of the bulbocavernosus and ischiocavernosus muscles radiate into its posterior part, and it ends anteriorly at the coronary sinus.

Beneath the fascia penis lie the **corpora cavernosa,** joined to it by the **subfascial connective tissue.** Each corpus is surrounded by a dense connective tissue **albuginea,** and the two unite in the middle line to form the **septum penis** (Pl. 64, Fig. 151). This is thickest behind and becomes increasingly thinner and more incomplete in front, so that here the two corpora cavernosa frequently anastomose. **Septa** extend from the albuginea into the interior of each corpus cavernosum and form by branching and anastomosis a system of **communicating hollow spaces,** which in general are smaller in the center of the organ, forming the central plexus, larger in the periphery, where they form the coarse cortical plexus, and smallest in the extreme periphery, creating the peripheral cortical plexus. They are lined with simple **flat *epithelium*** which resembles that of the vessels and lies directly on the septa. The latter consist of connective tissue reinforced with elastic, and contain bundles of **smooth muscular fibers** arranged quite irregularly. Most of the muscular bundles are contained in the septa of the corpus cavernosum penis, which are nevertheless thinner than those of the corpus cavernosum urethræ, for although the latter are poorer in muscular tissue they have their connective tissue more strongly developed.

The **arteries** of the penis are from the external and internal pudendal. The former supply the skin of the penis, the latter divides into the urethral, the bulbi

urethræ, the profunda penis, and the dorsalis penis. The first two enter the corpus cavernosum urethræ, the third the corpus cavernosum penis. The dorsal artery runs in the subfascial connective tissue to the glans and gives off numerous branches to the corpora cavernosa. After these have passed through the albuginea a part enter the above mentioned peripheral cortical plexus just beneath the latter, the spaces of which must be regarded as capillaries which open into the central plexus. The intermediate coarse cortical plexus is on the contrary supplied directly by other arterial twigs. Both the central and the coarse peripheral plexuses are of venous nature and are openly connected. A third part of the arteries are nutrient, run in the septa, and open into the central plexus. Finally little arteries, the arteriæ helicinæ, come from the profunda, project their incurved ends into the spaces of the plexuses and open into them.

All of the arteries of the corpora cavernosa have a powerfully developed circular musculature, and we also find in many of them ***cushionlike thickenings*** beneath the epithelium, which protrude into the lumen over wide areas and consist chiefly of fine, circular elastic fibers. Similar cushions occur also in the subfascial veins.

The efferent **veins,** venæ emissariæ, develop from the spaces of the plexuses in such a way that those coming from the central must pass through the lacunæ of the cortex. They assemble into the venæ profundæ penis and the unpaired vena dorsalis penis.

The **lymphatics** of the penis are superficial and deep. The superficial form plexuses in the entire cutis and assemble into subcutaneous longitudinal trunks that empty into the inguinal glands. Those of the glans and of the corpora cavernosa belong to the deep; they assemble into one dorsal subfascial trunk that also empties into the inguinal lymphatic glands.

The **nerves** of the skin of the penis come from the pudendal and the perineal. They form a large plexus in the cutis from which fibers ascend, part to penetrate between the cells of the epidermis, especially in the glans, while part enter special encapsulated end corpuscles situated in the papillæ of the corium. The nerves of the corpora cavernosa come from the sympathetic plexus cavernosus penis, which is a continuation of the plexus prostaticus, and anastomoses frequently with the dorsal nerve of the penis, which is a branch of the pudendal. Together with this plexus are cerebrospinal fibers that reach the penis from the lumbar plexus and are known as the nervi erigentes. They may receive a reflex stimulation from the skin of the penis that excites an erection. Nothing definite is known concerning the way in which they end in the erectile tissue.

VI. THE FEMALE GENITAL ORGANS

1. THE OVARY

The development of the ovary, the female germinal gland, from the **undifferentiated germinal rudiment** is materially different from that of the male germinal gland. The most important differences are that in the female there is no development of a typically glandular structure with a secretory and excretory system of ducts, and that consequently the reteblasts of the germinal rudiment and of the genital part of the Wolffian body are never able to play an important part, but portions disappear entirely, leaving insignificant traces of the remainder.

The first female characteristic of the genital rudiment is that the germinal epithelium sets up a lively proliferation and forms a thick cellular layer, the **cortex of the germinal rudiment,** which closes off the **medullary substance** from the mesenchymatous stroma enclosing the reteblast by a more or less distinct **primary albuginea.** While the reteblast gradually disappears the connective tissue of the medulla enters the cortex of germinal cells and breaks down its cellular mass into complexes ever becoming smaller, the so-called **ovarian vesicles.** This condition of proliferation of the germinal epithelium and subdivision of the material thus produced by connective tissue entering from the medulla is maintained until the third year of life. The ovarian vesicles consist of **germinal cells** or **oogonia,** and **undifferentiated epithelial cells,** derivatives of the epithelium of the cœlom. The cells produced by the division of the oogonia are the **oocytes,** equivalent to the spermatocytes of the testicle. While the latter very soon produce the prespermatids, and these the spermatids by reducing segmentation, the oocytes have a very long life. They become separated in the subdivision of the ovarian vesicle by the connective tissue and lie isolated in the latter surrounded by some undifferentiated epithelial cell. In the latter part of embryonal life these cells lie like an epithelium about each oocyte, the entire formation is enclosed in a connective tissue envelope and receives the name of **primary follicle.** The formation of these primary follicles extends from the primary albuginea toward the surface, so that about the third year of life the entire cellular material of the cortex has been transformed into primary follicles. When this condition is complete the primary albuginea disappears and there is developed in its place over the surface of the cortex, outside of the primary follicles, the **definitive albuginea,** a strong connective tissue, outside of which may be found the remains of the germinal epithelium as a single layer of cuboidal cells.

The **reteblast** never plays a great part in the ovary. It forms a network and unites with the **genital cords** that enter from the epithelium of the Wolffian body. The reteblast and genital cords, together with the masses of

mesenchyma situated here and the blood vessels that enter, form for a time the **rete ovarii,** but after the primary albuginea has disappeared the most of this **primary medullary substance** is taken up by the growing follicles to return after these are destroyed and to be transformed into the **secondary medullary substance.**

A part of the **tubules of the Wolffian body** with a piece of the **Wolffian duct** is preserved and lies on the completed ovary as the **epoophoron.**

Each **primary follicle** therefore consists of an ***oocyte*** surrounded by a mantle of epithelial cell, the ***follicular epithelium,*** and a connective tissue capsule, the ***theca folliculi.*** It begins to enlarge, grow, and mature in the last part of embryonal life, but the ovum does not attain its full maturity in the ovary, the final stage of the ripening process takes place in the efferent passages. Inasmuch as the separate stages of this process, with the exception of the final one, may be observed in the perfect ovary of the sexually mature woman, they will be described later. The greater part of the follicles that mature in the early years of life are destroyed. The discharge of the first mature ova from the ovaries marks the onset of puberty.

The ovary is covered externally by the **tunica albuginea,** an envelope composed of several layers of connective tissue fibers, the existence of which has recently been denied. Externally the albuginea is covered by a homogeneous, elastic membrane, which in turn is covered externally by a single layer of cuboidal, so-called **germinal epithelium.**

The parenchyma of the ovary is divided into a **cortex,** or **zona parenchymatosa,** and a **medulla,** or **zona vasculosa** (Pl. 64, Fig. 152). The two blend without a sharp line of demarcation and are developed through a **stroma** consisting of connective tissue fibers, in which follicles are embedded. These fibers are joined into bundles in the outermost cortex, are straight, run parallel to the surface, and interweave a great deal; in the deeper parts of the cortex they are more isolated and tortuous, run perpendicularly or obliquely to the surface and form a stroma that embraces the follicles. A very few **smooth muscle fibers** and cells are to be met with between the fibers and bundles of connective tissue, the cells most abundantly between the follicles. As we shall see later they arise from the cells of the walls of the follicle and are developed most strongly in the ovary of the child, to later gradually disappear. They contain granules of a yellow fatty body, **lutein,** and as a whole form the **interstitial ovarian gland.**

The fibers of connective tissue are thicker in the **zona vasculosa,** or **medulla,** than in the cortex, and interlace quite irregularly. The cortex is characterized by the follicles it contains, the medulla by its blood vessels, which enter at the hilum where this zone reaches the surface of the organ. The medulla is poorer in cells than the cortex. It is not unusual to meet with a plexus of cellular tubes at the hilum, that is nothing else than the remains of the rete ovarii.

The **follicles** lie enclosed in the connective tissue stroma of the cortex in such a way that the youngest stages are farthest out, the oldest farthest in (Pl. 65, Fig. 153). But as the follicle increases enormously in its ripening the most mature ones finally reach through the entire cortex. The great majority

of these follicles are destroyed in the course of the sexual life and only a small minority, about 0.6%, come to expulsion and full maturity.

The smallest follicles, the **primary,** are found in the outermost cortex beneath the above mentioned layer of connective tissue. They are very numerous and densely packed in the newborn, but their number diminishes as age increases. The follicle has a diameter of 60 to 70 μ, and consists of an ***oocyte*** and a single layer of flat ***follicular cells.*** The ***ovum,*** or ***oocyte,*** may have as great a diameter as 65 μ. A clear, reticulated protoplasm surrounds the nucleus, which averages 30 μ in diameter, and is commonly known as the **germinal vesicle.** It has a well developed basophilic framework of chromatin and a large nucleolus, or **germinal spot.**

The further development of the follicle that begins in the last part of embryonal life, but makes a special advance at the time of puberty, takes place first in the ovum, second in the follicular epithelium, third in the immediate vicinity, and leads to the formation of a vesicle 1.5 cm in diameter, filled with fluid, the **Graafian follicle.** We shall next discuss these changes more in detail.

The ovum increases considerably in size during the growth of the follicle, from a diameter of 60 μ to one of 200 μ. Therefore it increases three or four times in bulk, while the germinal vesicle grows at the most only one and a half times, so that the cell body has a considerably greater ratio to the nucleus in the mature than in the immature ovum. Minute **yolk globules** are deposited in this cell body, beginning from the nucleus in the meshes of the protoplasm, which finally occupy the entire body of the ovum, with the exception of a narrow, marginal zone. Then the germinal vesicle, which has been lying in the center, takes an eccentric position and its chromatin steadily loses its basophilia until it becomes oxyphilic. Finally the ovum is surrounded by a homogeneous capsule, the **zona pellucida,** in the formation of which the substance of the ovum and the follicular epithelium are probably uniformly involved.

The **follicular epithelium,** which consists at first of a single layer of flat cells, has a lively growth. The cell becomes cuboidal, then cylindrical, and then begins to divide, a process that it repeats many times, so as to form about the ovum a coat composed of many layers of cells, the follicular epithelium, or the **membrana granulosa.** After the follicle has attained the size of 200 to 300 μ **hollow spaces** appear in the membrana granulosa, starting in the portion of the membrane that lies next to the surface of the ovary by the vacuolization and the rendering fluid of the contents of its cells. The cavity has at first the shape of a cap with its convex side outward, its concave side inward and turned toward the ovum. By gradual enlargement a large cavity finally develops which is lined by several layers of granulosa epithelium, and into which projects at a certain place an epithelial elevation, the **cumulus ovigerus,** enclosing the ovum.

The *changes in the vicinity of the follicle* consist of the development of a capsule about the follicle from the surrounding ovarian stroma, the **theca folliculi.**

Such a **complete follicle** has a size of from 0.5 to 1.5 cm, and is en-

wrapped by the **theca folliculi,** of which we may distinguish two parts, the ***theca externa*** and ***theca interna.*** The former is composed of many interlacing connective tissue fibers, the latter of large spindle-shaped, or more roundish cells packed closely together. They contain minute drops of fat as well as granules of a yellow lipoid, lutein, and are known as the **thecal lutein cells.** Internally the theca interna is bounded by a structureless **vitreous membrane,** the **lamina vitrea.**

The follicle is lined by several superimposed layers of **follicular epithelium** that rises in the part looking toward the medulla into the **cumulus ovigerus** protruding into the cavity of the follicle. The deepest layers of cells, those next to the lamina vitrea, as well as those directly surrounding the ovum, are cylindrical; all the rest are polyhedral. The cells anastomose by means of fine protoplasmic processes, so that the entire follicular epithelium is a synctium.

The cavity of the follicle contains the **liquor folliculi,** of which from 1 to 4% of the constituents are solid, including albumin and pseudomucin.

As a rule the **ovum** lies alone in the **cumulus ovigerus;** it is seldom that we find several ova in the human follicle, as we do in that of the rabbit. It has a diameter of about 200 μ, and is encased in the **zona pellucida,** which averages 12 μ in thickness, and in which a fine, radiating striation may be perceived. The body of the ovum has a very fine alveolar structure and contains in the alveoli the very minute **yolk globules,** that occupy the entire body, with the exception of a narrow, peripheral zone. The eccentrically placed **germinal vesicle** has a diameter of about 25 μ and contains the **germinal spot,** about 5 μ in diameter, and a framework of chromatin, both of which are oxyphilic.

As soon as the follicle has enlarged enough to reach the albuginea a degeneration takes place in the neighboring parts of its wall and the internal pressure increases at the same time until a rupture takes place into the abdominal cavity. The ovum, surrounded by a crown of follicle cells, the **corona radiata,** is seized by the fimbriæ and guided into the Fallopian tube, where it passes through its final process of maturation, and where fructification takes place. This ripening process has not yet been observed in the human ovum, but consists of the expulsion of **directing bodies,** which become two in number through two successive segmentations, the last of which is a reducing division, as separate little corpuscles and die, so that an essential difference is furnished herein from spermatogenesis. In the latter each *spermatocyte provides four spermatozoa,* while in oogenesis only *one ovum capable of fructification originates from each oocyte.*

The cycle of **ovulation,** the expulsion of the ovum, does not always seem to proceed in the same way. In very many cases ovulation takes place at regular intervals, so that an ovum is expelled about every twenty-eight days, probably about twelve days before the onset of **menstruation,** but in other cases ovulation takes place irregularly, by fits and starts, although the menstruation may follow its regular cycle. Ovulation comes to an end with the cessation of menstruation, the **menopause,** about the forty-fifth year of age. The store of ova or follicles is now exhausted, and the senile ovary is practi-

cally a body of connective tissue that no longer has follicles, contains only scanty traces of yellow bodies, and whose vessels degenerate more and more.

Soon after the ovum has left the cavity of the follicle the walls of the latter collapse and from it develops the **corpus luteum.** If pregnancy ensues a large ***corpus luteum verum*** results that lasts several months, otherwise a small ***corpus luteum falsum*** is formed that soon disappears. At the height of its development the corpus luteum consists of **lutein cells,** of connective tissue fibers that twist about these cells, and of blood vessels from the theca that run between them. The luteum cells are 50 μ or less in diameter, each with a large spherical nucleus and a vacuolized protoplasm that contains **granules of lutein** in the vacuoles. Views differ as to their origin, but the theory most widely accepted is that they originate through proliferation of the granulosa cells. In the center of the body there is at first a cavity filled with follicular fluid and extravasated blood, but this is soon replaced by connective tissue. As soon as the height of the development of the corpus luteum is passed the lutein cells degenerate and break down, the connective tissue shrinks, and the blood vessels collapse. The entire body loses its yellow color, sinks together and is now known as the **corpus albicans.**

Probably the lutein cells of the corpus luteum and the cells of the interstitial germinal gland are equivalent. They produce a substance that enters the blood and is perhaps of importance in the implantation of the ovum in the uterine mucous membrane.

The great majority of the follicles formed in the ovary do not attain full development, but pass away prematurely. While this may be their fate at any stage, it is chiefly so in middle life, when the follicles have well developed thecas, but are without cavities. This is called **atresia of the follicles.** Degenerative processes play a part, seize first upon the ovum, then upon the follicular epithelium, and destroy both, while the fibrous and the cellular constituents of the theca proliferate. The cells of the proliferated theca interna then form what we have learned to know as the interstitial ovarian germinal gland enveloped in connective tissue fibers. They resemble in all essentials the lutein cells of the corpus luteum.

The **arteries,** several large branches of the uterine and ovarian, enter at the hilum, take a very tortuous course, branching continually, to the margin of the medulla, where they form a dense vascular plexus, from which arteries branch into the cortex to form fine meshed capillary plexuses about the follicles and in their thecas. The veins form an extensive plexus in the medulla, but particularly in the hilum, that gives the tissue a spongy appearance.

The **lymphatics** weave about the follicles in like manner as the blood vessels and form two plexuses, one superficial, beneath the albuginea, and one deep, at the border between the medulla and the cortex. Little trunks pass from this into the medulla to anastomose again in the hilum into a plexus. The efferent vessels empty into the aortic lymphatic glands.

The **nerves,** that come from the spermatic and renal, enter at the hilum with the blood vessels, form a wide plexus in the medulla, from which fibers pass into the cortex and twine about the follicles. The majority are non-medullated, the minority medullated.

From the rudimentary organ near the ovary we have the **epoophoron,** the residue of the genital portion of the Wolffian body. Its canaliculi have a cuboidal or ciliated epithelium which rests on a connective tissue propria. A circular layer of smooth muscle fibers is often added externally.

The **paroophoron,** lying in the broad ligament between the branches of the internal spermatic artery, is a residue of the caudal portion of the Wolffian body, and in well marked cases it may be seen how this is composed of the capsule of the Wolffian body and convoluted tubules with cuboidal epithelium. Both of these pass away in later life and become cysts with irregular masses of epithelium.

The **pedunculated hydatids** also are derived from the Wolffian body, are connected with the epoophoron in many cases, and have a cuboidal, or a cylindrical epithelium.

2. THE FALLOPIAN TUBE

In males the Wolffian duct carries away the germinal products, but in females this duty devolves upon **Mueller's duct,** the development of which has been described already. It runs at first to the lateral side of the Wolffian duct, crosses it farther toward the cauda, and comes to lie close to its partner of the opposite side, each flanked laterally by the Wolffian duct. The most caudal portions of all four are included in the **genital cord.** A fusion of the two Mueller's ducts takes place in both sexes, but it extends considerably farther cranially in the female. The fused portion forms the **uterovaginal canal,** the free cranial portion on each side the **oviduct,** or **Fallopian tube.** The epithelium of the latter consists at first of several rows of cylindrical epithelium, later becomes simple cylindrical, and gains a ciliated margin toward the end of pregnancy. At the beginning of the fourth embryonal month the surrounding mesenchyma forms several longitudinal folds covered with epithelium that protrude into the lumen of the oviduct. Secondary folds grow out from these primary ones and straighten the lumen very much. About the same time that these folds are formed smooth muscle fibers appear in the mesenchymatous wall of the oviduct, which are at first circular in arrangement and have longitudinal muscular bands added later. The formation of folds in the mucous membrane extends not only to the entire length of the oviduct, but extends to the open cranial end, from which the folds grow out in the form of several fingers, the **fimbriæ.** They lie close to the young ovary, at first on its lateral, later on its medial and dorsal sides.

The **mucous membrane** of the complete oviduct is thus characterized by its marked **folds,** which constantly increase in height from the ostium uterinum through the isthmus to the ampulla, where they are very high, protrude into the axis of the canal, and have numerous secondary folds that fill the lumen completely (Pl. 65, Fig. 154). At the ostium abdominale the mucous membrane continues over the fimbriæ, covered by a moderately high, 15 to 20 μ, simple cylindrical **epithelium.** Two sorts of cells may be distinguished, one broad and clear, the other narrow and dark, each of the former surrounded by an areola of the latter (Pl. 65, Fig. 155). The broad clear cylindrical

cells are provided with **cilia** that have distinct basal corpuscles at the ends implanted in the surface of the cell. The ciliary movement is toward the ostium uterinum. The nucleus lies in the center of the cell. **Secretion granules** may be seen in the cell bodies, that vary in development and probably consist of mucigen. Part of the narrow cells are filled with such granules, part are not, but they have no cilia. Comparative studies of the tubal epithelium of various animals have shown that they issue from the ciliated cells, the ciliary margins of which have been destroyed by the pressure of the secretion. The cell then collapses and exhibits in this condition only a double central body. Later the ciliary margin is reformed and the cell begins anew the elaboration of secretory material.

The epithelium rests directly on the richly cellular **propria,** there being no basal membrane. The propria forms the basis of the primary and secondary folds and is covered by a **muscularis mucosæ,** the fibers of which run longitudinally. The **submucosa** is poorer in cells than the propria, contains elastic fibers, and in it run the larger vessels and nerves. The propria and submucosa are permeated uniformly by elastic fibrous networks, which are better developed in the adjoining muscularis. The **muscularis** is strongest in the isthmus and is composed of an inner circular, and an outer longitudinal layer of smooth muscle fibers.

Externally the tube is covered by **peritoneum,** the subserosa of which contains very strong elastic fibrous networks and smooth muscle fibers. The serous passes over into cylindrical epithelium on the fimbriæ.

The **arteries** come from the uterine, branch in the subserosa, pass through the muscularis, and form capillary plexuses first in the latter, then in the submucosa and propria. The **veins** form three plexuses in the wall of the tube, one submucous, one intramuscular, and one subserous. The last is best developed on the lower border of the tube and opens into the uterine, internal spermatic, and epigastric veins.

The **lymphatics** form three similar plexuses and assemble into several little trunks that unite with those of the ovary.

Part of the **nerves,** which enter with the vessels, are branches of those of the uterus, part of those of the ovary, form plexuses like those of the vessels, and end in the epithelium and on the muscles. Ganglia are present in the plexuses.

The Fallopian tube conducts the ovum from the ovary to the uterus, its place of implantation. The fimbriæ near the ovary probably produce a strong current by means of the cilia of the epithelium, which guides the ovum when it comes forth from the ovary into the ostium abdominale. Within the tube the final ripening and the fructification take place.

3. THE UTERUS

As stated above, the uterus originates through the fusion of the ***caudal sections*** of both ***Mueller's ducts*** into the genital cord, or, to put it more accurately, from the ***uterovaginal canal,*** a tube lined with cylindrical epithelium and encased in mesenchymatous tissue, which divides cranially into the

two Fallopian tubes, and opens caudally into the **urogenital sinus** in common with the urethra. It lies to the dorsal side of the latter and of the bladder. Changes appear in this uterovaginal canal in the fourth month of pregnancy, such that the caudal half is closed by a proliferation of its epithelium and is bent simultaneously at an obtuse angle to the cranial portion. Soon afterward a differentiation takes place in the cranial portion of **smooth muscle fibers** in the mesenchymatous envelope, and from this develops a muscular organ with a simple lumen like a canal lined with cylindrical epithelium, the **uterus.** Its demarcation from the vaginal portion by an epithelial proliferation takes place at the end of the fifth month in such a way that starting somewhat caudally from the beginning of the occlusion the epithelium advances cranially in the form of a cuff that surrounds the caudal end of the uterus. When the central parts of the epithelial vagina degenerate to form a lumen, this formation extends into the cuff so that the caudal end of the uterus protrudes for a distance into the vagina as the **portio vaginalis uteri.** A residue of the epithelial degeneration is a stratified flat epithelium that lines all parts of the canal, covers the outer surface of the portio, and passes over into cylindrical epithelium at the entrance to the uterus, the os uteri.

The uterus of the sexually mature female is a very strong muscular organ, the wall of which presents from within outward a **mucous membrane,** or **endometrium,** a **muscularis** or **myometrium,** and a **peritoneal coat** or **perimetrium** (Pl. 66, Fig. 156). The mucous membrane of the uterus is continuous with that of the Fallopian tubes at their mouths, and with the vaginal portion at the os uteri externum. It is about 1 mm thick, without folds in the body, but with a system of folds in the cervix on the rectovesical wall, the arbor vitæ, a longitudinal ridge with several lateral ones branching from it at an angle. The longitudinal fold marks the place where the two Mueller's ducts became fused.

The **mucous membrane** is covered by a single layer of ***ciliated cylindrical cells*** that are from 20 to 30 μ long. Each cell has an ovoid nucleus, situated at its base, and a quite feebly basophilic protoplasm. The relatively short cilia are implanted in the free surfaces of the cells, each with a basal nodule. The epithelial cells are rather higher and the cilia somewhat longer in the cervix, otherwise they are exactly like those in the corpus. The child's uterus has a simple cylindrical epithelium without cilia, and the latter disappear again after the menopause, after which the cells decrease much in height (Pl. 66, Fig. 157).

The epithelium rests on a homogeneous **membrane propria.**

The powerfully developed **propria** is of adenoid nature. It is a network of anastomosing stellate and spindle-shaped cells which is densest beneath the epithelium. The collagenous fibers are extremely fine and are mixed with elastic fibers. Lymphocytes lie in the meshes of the reticulum.

The propria contains the **uterine glands,** which also penetrate into the muscularis. They are simple or slightly branched invaginations of the uterine mucous membrane, which under normal conditions are from 100 to 200 μ apart and from 1 to 2 mm long (Pl. 66, Fig. 156). Their epithelium resembles that of the surface, but gives a much more distinct mucous reaction, although the

granules of mucigen cannot be demonstrated in the cells themselves. Secretion is always to be found in the lumen of the gland in the form of threadlike masses, which are carried by the current produced by the cilia into the cavity of the uterus. The **cervical glands** in the cervix are alveotubular and of greater extent (Pl. 67, Fig. 158). The epithelium consists of ciliated cylindrical cells, mixed with true goblet cells. While the cervical glands appear in the fifth month of pregnancy, the uterine ones develop about the time of birth, or during childhood.

The **muscularis** forms the main part of the wall of the uterus and consists of bundles of smooth muscle cells about 50 μ long, surrounded by an envelope of elastic and collagenous fibers. The following layers are commonly distinguished from within outward. The ***stratum submucosum,*** a thin, slight layer of longitudinally running muscular bundles; the ***stratum vasculare,*** the most powerful layer, in which the bundles take for the most part a circular course, but are split up into many groups by others that run longitudinally, and containing many large blood vessels, as implied by its name; the ***stratum supravasculare,*** which is not very powerful and contains an equal number of bundles that follow a longitudinal and a circular course; and the ***stratum subserosum,*** the outermost layer, which contains only longitudinal bundles. As already stated, much elastic and collagenous tissue is found between the muscular bundles and fibers. The elastic fibers form a stratum that separates the muscularis from the subserosa and pass from this into the subserous and supravascular strata. The vessels that radiate into the stratum vasculare from the adventitia are numerous, while they are very few in the stratum submucosum.

The **serosa** rests immediately upon the above mentioned elastic stratum.

During the period of sexual activity the wall of the uterus exhibits regularly recurring transformations that are called **menstrual. Menstruation** begins with puberty, in our latitude about the age of fourteen or fifteen, recurs every twenty-eight days and ceases about the forty-fifth year in the so-called **climacteric,** or **menopause.** When pregnancy supervenes menstruation is arrested until after parturition and the period of lactation. The external manifestation of menstruation is an outflow of blood mixed with uterine mucus from the vagina. The entire process may be divided into four stages which correspond to the changes that take place in the uterine mucous membrane, an ***interval*** of fourteen days, a ***premenstrual period*** of seven days, a true ***menstrual period*** lasting three days, and a ***postmenstrual period*** of four days.

The condition of the uterine mucous membrane described here as normal is found only in the postmenstrual period. On the last day of this period and during the interval there is a considerable thickening of the mucous membrane associated with a marked growth of the uterine glands. Very many karyokinetic figures may be seen in the nuclei both of its cells and of those of the propria. The glands, which have become corkscrew-shaped, now begin to secrete and the process enters the premenstrual period, in which the glandular cells enlarge greatly, become high cylindrical and project far into the lumen of the gland. The glandular tubes may be thrown into little folds, giving the glands a sawlike, or bushlike form. The cells in the propria become much swollen, rounded, and

gathered into larger complexes. Just before the onset of the menstrual period the process of secretion reaches its acme and signs of degeneration begin to appear, first in the nuclei, and then in the glandular cells. The blood vessels are much dilated, the wall is loosened up, great numbers of leucocytes enter the stroma, and finally there comes a gush of blood and an expulsion of the loosened up mucous membrane, wherewith the process enters the menstrual period. The separation takes place within the deep layers of the mucous membrane, leaving the basal layer next to the muscularis. The shreds of mucous membrane are either extruded with the blood by the contraction of the muscles of the uterus, or break down in the uterine cavity and are removed by phagocytosis. Regeneration sets in immediately from the preserved portions of the glands with a lively multiplication of cells. The remains of the mucous membrane thus becomes covered by a new epithelium and grows again very rapidly to its former thickness.

The processes that take place in this menstrual cycle render the mucous membrane of the uterus fitted for the reception of an impregnated ovum. If none such is present the proliferated mucous membrane is cast off, but if an ovum has become impregnated in the Fallopian tube it nests in the proliferated mucous membrane and the latter becomes the decidua graviditatis.

The **arteries** of the uterus come from the uterine and the ovarian. They enter the lateral surfaces, pass through the external muscular layers, and form an extensive plexus in the stratum vasculare, from which part of the twigs go to the muscles, part to the mucous membrane, where they form a dense capillary plexus about the glands, reaching to the epithelium. The **veins** that arise therefrom are relatively small, anastomose much with one another, thus forming several plexuses in the uterine wall, and empty into the uterine and uterovaginal veins.

The **lymphatics** are not yet known with perfect certainty. It is a question whether any provided with walls exist in the uterine mucous membrane, but such are certainly present in the musculature and the subserosa. The efferent vessels, divided into several little trunks, pass out of the cervix and the corpus to open into the iliac lymphatic glands.

The **nerves** form an extensive plexus provided with numerous ganglia on the lateral surfaces of the uterus. They are mainly sympathetic, associated with a few medullated fibers, and come from the hypogastric plexus and the sacral nerves. Within the walls of the uterus they form a large plexus, the branches of which go to the muscles and vessels, to end between the epithelia of the glands and of the surface. Ganglion cells do not appear to be present in this plexus. Contractions take place in the uterus after destruction of the spinal cord and are influenced only a little by the central organ.

4. THE VAGINA

The embryology of the vagina was discussed under the preceding subject. After the occlusion of its lumen by proliferation of epithelium the epithelial mass constantly increases in circumference, its caudal end alone remaining thin and narrow, so that after the restoration of its lumen the vagina is relatively

wide and opens outward through a narrow aperture surrounded by a fold of mucous membrane, the **hymen.** Originally both the vagina and the urethra open at an acute angle into the urogenital sinus, but toward the end of the fourth embryonal month the now relatively short sinus increases much in breadth sagittally and becomes the vestibule of the vagina, while the openings of the urethra and vagina separate more and more, the latter turning toward the anus, until both open separately into the vestibulum vaginæ.

The vagina is lined by a **mucous membrane** that lies in numerous transverse folds or rugæ (Pl. 67, Fig. 158). They unite on the rectal and vesical walls, like the system of folds in the cervix, the longitudinal ones, the columnæ rugarum, marking the original construction from two adjoining tubes. It is covered by a much stratified **flat epithelium,** about 200 μ thick, in which the beginnings of cornification may frequently be seen. This epithelium continues in the vault of the vagina over the portio vaginalis, covering it as far as the external os where it changes rather suddenly into the cylindrical epithelium of the uterine mucous membrane. At the entrance to the vagina it is continuous with the similarly constructed epithelium of the vaginal vestibule.

The **propria** of the vagina juts out with numerous high, slender papillæ into the epithelium, passing through as much as three fourths of its thickness. Its connective tissue is very dense, finely fibrous, and abundantly supplied with elastic fibers. Follicular accumulations of lymphocytes are formed in many places. Glands are totally wanting. The propria forms the basis of the system of folds and of the hymen, which is nothing else than a special high fold of mucous membrane that forms its outer limit.

The adjacent **submucosa** is materially looser than the propria, and joins the latter to the **muscularis,** the smooth fibers of which are a continuation of the longitudinal fibers of the stratum vasculare. To the inner side of the thick longitudinal stratum we find some scanty circular fibers. Numerous elastic fibers run between the bundles.

Externally to the muscularis comes the connective tissue **adventitia,** which unites the vagina with the paravaginal tissues.

The **arteries** come from the vaginal and the median hemorrhoidal. They run first in the adventitia, thence send branches into the musculature and mucous membrane, where they form a capillary plexus that stands out particularly well in the papillæ of the propria. The **veins** form a plexus which is always denser in the deeper parts, and empties into the uterovaginal and vesical plexuses.

The **lymphatics** form a plexus like that of the veins. They assemble into several little trunks, the lower of which go to the inguinal, the middle and upper to the hypogastric and iliac lymphatic glands.

The **nerve fibers** coming from the uterovaginal plexus and the sacral nerves form a plexus studded with ganglia in the wall of the vagina. Their twigs end free between the epithelial cells in the mucous membrane, and on the muscular fibers and the vessels.

5. THE EXTERNAL FEMALE GENITAL ORGANS

The external female genital organs develop from the ***undifferentiated rudiment,*** as we have already seen. The **genital eminence,** which becomes the penis in males, attains no such dimensions in females, but has in general the same structure and is known as the **clitoris.** The **genital folds** extending out from it, which in man serve to close in the urethra, grow in woman into two folds of skin that border the vestibule of the vagina, the **labia minora,** and form above the **frenulum clitoridis** and the **præputium clitoridis.** The **genital prominences,** which in man go to form the scrotum, enlarge in woman into the **labia majora.**

a. The Vestibule of the Vagina

The vestibule of the vagina, situated between the labia minora, is the sagittally broadened urogenital sinus and contains in its wall a pair of erectile bodies, the **bulbus vestibuli,** which corresponds to the corpus cavernosum urethræ of the man. It is supplied with blood by the external pudendal artery and consists essentially of a dense venous plexus.

The **glandulæ vestibulares** open into the vestibule. These are two ***glandulæ vestibulares majores,*** or ***Bartholin's glands,*** and several ***glandulæ vestibulares minores.*** The former lie on each side just beneath the posterior end of the bulbus vestibuli, and are analogous to, as well as constructed the same as Cowper's glands in the male. The excretory duct is lined with stratified flat epithelium and opens on each side into the lower half of the vestibule at the base of the labia minora.

The glandulæ vestibulares minores are little, simple or branched tubes found between the introitus vaginæ and the orificium externum urethræ and about the hymen, and are lined with cuboidal mucous cells.

b. The Clitoris

The clitoris corresponds embryologically to the penis, with the exception of its urethral portion, and like it has two **corpora cavernosa,** a **glans,** and a **prepuce** formed from the labia minora. The structure of all of these scarcely differs from that of the corresponding parts in the male. The arteries come from the pudendal; the venous blood collects into the vena dorsalis clitoridis. The skin of the clitoris is very richly supplied with sensory nerve fibers, part of which end free in the epithelium, part in capsulated corpuscles.

c. The Labia Minora

The labia minora resemble the skin in structure. They consist of connective tissue richly provided with elastic, and containing smooth muscle fibers. Numerous high papillæ covered with stratified flat epithelium are found. The labia minora have no hairs, only a few sweat glands, but many sebaceous glands. Blood vessels are numerous, and large veins in particular are present, so that a certain erection takes place with sexual stimulation, as in the clitoris. The nerve supply is the same as that of the latter.

d. The Labia Majora

The labia majora have the same structure as the minora, and differ from them only in the possession of numerous hairs, unusually long sweat glands and much more horny epithelium. The subcutaneous connective tissue contains great masses of fat, which together form the adipose tissue of the labia majora.

VII. THE ORGANS OF MOVEMENT

1. THE MUSCLES

Although each of the three primitive blastoderms is able to produce muscular fibers, yet most of the muscles originate in the **mesoderm.** Here we find the **myotomes,** coming from the primitive vertebræ, from which are derived the great bulk of the muscles of the body. They form rows one behind another in the embryonal body, separated by **myosepta,** and consist of cylindrical cells, the **myoblasts.** The latter provide the muscle fibers and are probably united at first into a synctium by protoplasmic bridges that are not confined to any one myotome, but anastomose the myoblasts in neighboring myotomes by passing through the myosepta.

The nuclei within the myoblasts multiply through indirect segmentation. The protoplasm contains many coiled threads, the chondrioconts, and little granules, the chondriosomes. The chondrioconts group themselves longitudinally one after another and form the **myofibrils,** which pass from one myoblast into another and also join neighboring myotomes together. At first they are smooth, but later thickenings appear at certain intervals, from which develop short rods intercalated in the course of the fibrils, and so produce their isotropic and anisotropic segments. The formation of fibrils begins in the periphery of the cell and soon extends to the entire cell body.

After all of the myoblasts of the myotome have become fibrillated and transformed into muscular fibers, many of them degenerate and the remainder multiply by longitudinal fissuration. The **muscular fibers** thus produced are originally all of the same diameter, but later some increase, while others decrease in circumference.

The individual **muscles** may originate either through the fusion of myotomes that are placed one behind another, or through the outgrowth of myotomes and groups of myotomes, while still others come from mesoderma that is not articulated into myotomes.

Entire **groups of muscles** become encased and separated from their neighbors by **fasciæ,** dense, firm membranes that consist of several layers of connective tissue. Each layer is composed of bundles of connective tissue fibers with numerous elastic fibers between them. The direction of the fibers is the same in each layer, but varies in the different ones.

Each individual muscle is enclosed in a **perimysium externum,** which consists of bundles of connective tissue, mixed with elastic fibers, that are longitudinal for the most part, and contains the larger vessels and nerves that enter the muscle (Pl. 68, Fig. 159). The perimysium externum sends into the muscle many anastomosing septa that have the same structure but a smaller quantity of elastic tissue. These together form the **perimysium internum,** and divide the entire mass of the muscle into bundles that successively become

smaller and smaller. Vessels and nerves run in these connective tissue septa, divide repeatedly, and finally reach the **primary muscular bundles.** Each of these consists of a varying number of **muscular fibers,** encased and separated by connective tissue fibers that branch into the bundles from the primary septa.

The **arteries** commonly enter the muscle perpendicularly to the course of the fiber and split up into many branches within the perimysium internum. The smallest ones enter the primary muscular bundle perpendicularly and break up here into their terminal twigs, which form a long capillary plexus about the muscular fibers. The **veins** are usually two in number, are provided throughout with valves and generally follow the course of the arteries.

The **lymphatics** accompany the blood vessels and probably also form plexuses in the primary muscular bundles.

The **nerves** of the muscles consist of medullated fibers that come for the most part from the anterior roots of the spinal cord; a minority are sensory and come from the spinal ganglia. A smaller number of nonmedullated sympathetic fibers are always present and are destined for the vessels. Within the perimysium internum the nerve trunks break up into twigs that constantly become finer, which at last enter the primary bundles. They usually cross the muscular fibers obliquely and give off their branches at an acute angle (Pl. 69, Fig. 161). A medullated **motor nerve fiber,** often accompanied by a sympathetic one, extends to each muscular fiber and forms on it a **motor end plate.** The axis cylinder suddenly decreases much in thickness near the end plate, often splits into two branches and passes over into an antlered formation within the sarcolemma (Pl. 70, Fig. 162). This terminal antler is composed of fibrils that run at first parallel to each other and then bend about to form loops at their ends. The medullary sheath is lost shortly before the entrance of the fiber into its end plate, while the sheath of Schwann on the contrary is retained and blends with the sarcolemma. The terminal antler lies in the substance of the muscular fiber at a place free from myofibrils formed from the sarcolemma, the **granulosa,** or **sole plate.** Many nuclei are to be found between the antlers and in their vicinity. The end plate often bulges the muscle fiber outward, for which reason it has been called the neural prominence. Each muscular fiber contains only one end plate, as a rule.

The slightly tortuous **sensory nerve fibers** often accompany the muscular ones for long distances, giving off here and there fine, nonmedullated varicose lateral twigs that end with little thickenings on the fiber (Pl. 71, Fig. 163). Another part of the sensory fibers end free in the connective tissue of the perimysium with branches that resemble antlers, and there are still other fibers that enter encapsuled corpuscles.

The perimysium internum contains in addition to nerves and blood vessels the so-called **muscle spindles** (Pl. 68, Figs. 159 and 160), which are to be found in almost all the muscles of the human body, with the exception of the laryngeal and ocular, varying in number and development, and ranging in length from 2 to 10 mm. Each spindle is surrounded by a **connective tissue sheath,** and has one or more enlargements in its longitudinal section. Internally the sheath has a coating of branching cells that anastomose with their

processes and passes through the interior in which striated **muscle fibers** run longitudinally, various numbers entering at one end of the spindle and leaving it at the other. On the way these fibers divide dichotomously several times in succession, anastomose with their twigs, and thus form a **network** with fairly thin muscular trabecula within the spindle. In many places the nuclei of these trabecula are packed very closely together, so that the muscle fiber is completely filled with them. They lose their chromatin almost entirely and become little vesicles that are given a polyhedral form by the close compression. What remains of the interior of the spindle is filled with an albuminous fluid. At least two **nerve fibers** enter each spindle, one or more ***sensory,*** the others ***motor,*** and nonmedullated fibers also may be observed in them. The sensory fibers form extensive endings about the muscle fibers, twining about them in spirals and giving off lateral twigs that end on them in the form of plates or hooks. The motor fibers terminate with typical end plates. Opinions are still divided concerning the **special function of the muscle spindles,** yet they are doubtless important ***receptory end organs,*** which perhaps appertain to the muscular sense, and to the adjustment of the condition of contraction of the muscle in question.

2. THE TENDONS

The muscles are attached to their places of origin and insertion by tendons that vary extremely in form. Each tendon is surrounded by a **peritenonium,** which corresponds to, and has the same structure as the perimysium. It sends septa into the organ that divide it into bundles of tendon substance ever growing smaller, as in the muscle. The smallest, the **primary bundle,** consists of quite a number of **tendon fibers** with **tendon corpuscles** between them, as described in the first part of this work (Pl. 13, Figs. 39 and 40). The tendon fibers run without interruption through the entire tendon and fuse at their distal ends with the connective tissue of the periosteum or perichondrium. At their proximal ends they unite with the muscle fibers (Pl. 71, Fig. 164). The nature of this union is the subject of a lively scientific discussion. One theory is that the tendon fibrils perforate the sarcolemma and are continuous with the muscle fibrils. Other authors maintain that the sarcolemma separates the muscle from the tendon fiber completely, that the last is luted firmly to the first by a special substance, and that the peripheral fibrils of each tendon fiber are continuous with the connective tissue fibers of the perimysium internum.

The **blood supply** of tendons is on the whole very scanty. The vessels enter the septa from the peritenonium and break up into capillaries. The interior of the primary bundle is nonvascular. The blood vessels are accompanied by **lymphatics**.

The tendon is naturally supplied with **sensory nerves** alone, which are fairly numerous, part of them ending in Pacini's corpuscles, part in organs that greatly resemble muscle spindles. The **tendon spindles** lie in the peritenonium or in the coarser septa, have capsules, and are passed through by tendon fibers on which the nerves end with extensive, bushlike arborizations (Pl. 71, Fig. 164).

Wherever tendons pass over joints they are surrounded by special **tendon sheaths** to enable them to glide easily. The tendon sheath is a hollow cylinder that is invaginated from below about the tendon, so that the latter comes to lie in its axis and is attached to it by the **mesotendon.** The sheath consists of a thick **fibrous,** and a thin **mucous layer,** the former being the outer envelope, while the latter covers the tendon with its visceral layer and the inner surface of the fibrous sheath with its parietal. Between the visceral and parietal layers is the **cavity of the sheath,** filled with a viscous fluid. The mucous layer consists of loose connective tissue with many fibroblasts that form an epitheliumlike coat, interrupted in many places, toward the cavity of the sheath.

3. THE BONES

The development of bone was dealt with in extenso in the early part of this work. Bones are covered externally with **periosteum** which is divided into two layers. The outer of these, the **adventitia,** consists of bundles of connective tissue that cross and interlace, and have running between them many elastic fibers and blood vessels. The inner layer, the **fibroelastica,** is distinguished from the preceding by its looser structure, the fineness of its bundles of connective tissue, the abundance of elastic fibers and of cells, and the small number of its blood vessels. On its inner surface, next to bone, it is covered by a discontinuous layer of cuboidal cells from which the **appositional growth** and the **regeneration of bone** proceed and thus become osteoblasts at a given time. The adventitia connects the periosteum with the neighboring parts, particularly with the tendons of origin and insertion of the muscles, while the fibroelastica is joined to the bone substance itself. This union is effected by the incoming and outgoing blood vessels, but mainly by bundles of connective tissue that bend at right angles from their courses, which in general is parallel to the surface, and enter the bone substance, where we have learned to know them as **Sharpey's fibers.** Elastic fibers also may accompany the bundles of connective tissue from the periosteum into the bones.

The bones themselves are composed in their outer segments of ***compact*** bone substance traversed by Haversian canals, and changes internally into the ***spongy bone substance,*** a network formed from thin, anastomosing leaves of bone. The spongy leaves and trabeculæ contain no Haversian canals or Haversian lamellæ, but only basic lamellæ. In the long bones the compact cortex is thickest in the middle of the diaphysis and tapers uniformly toward each end. In the flat bones the compact substance occupies a much greater space. forming thick outer and inner tables joined together by a thin spongiosa here called the **diploe.** The arrangement of the trabeculæ in the spongiosa is characteristic in each bone and is in accordance with the laws of mechanics.

The cavities of the spongy substance and the **medullary cavity** of the bone, which lies in the center of the spongiosa, are filled with **bone marrow.** In childhood this is a soft mass stained red by the blood it contains, and is known as the ***red bone marrow.*** This undergoes many changes in later childhood that lead chiefly to the production of fat and transform it into the ***yellow, fatty marrow.*** In adults the medullary cavities of the large, hol-

low bones are filled with fatty marrow, while the spongiosa of the smaller bones contains red marrow. Yet the former may change back into red marrow at any time, especially after great losses of blood. In old age, or sooner under pathological conditions, a mucous degeneration of the fat takes place in the fatty marrow and gives rise to the so-called ***gelatinous marrow.*** Under other conditions its fibrous constituents may proliferate, and then we speak of a ***fibrous marrow.***

The basis of the red marrow is a **reticulated tissue** that fills the cavities of the bone and is permeated with numerous blood vessels. The fibers are very fine, rather coarser about the vessels, and form plexuses. Microchemically they resemble the fibers of the reticulum of the lymphoid organs. The cellular elements of the marrow lie within their meshes, partly within delicately walled blood vessels, partly free, and have important relations to the formation of the blood. They are:

1. The **medullary cells,** or **myeloblasts,** medium sized cells with large nuclei and narrow, weakly basophilic margins of protoplasm. They originate in loco through segmentation and are metamorphosed connective tissue cells from the beginning. They may be transformed in two ways. They may wander into the blood vessels and become

2. **Erythroblasts.** These multiply very much within the vessels, begin to elaborate hæmoglobin, lose their nuclei, and so become erythrocytes which are carried away by the blood current. The red bone marrow must be considered the most important center for the formation of erythrocytes in postfetal life. The other way in which myeloblasts undergo transformation is for them to elaborate granules in their bodies and so to become

3. **Granular leucocytes.** We find in the marrow both neutrophilic and eosinophilic, as well as plasma cells and mast cells, the characteristic features of which have already been described. Part of these likewise enter the circulation, and the bone marrow consequently is to be regarded as a center for the formation of leucocytes.

4. **Giant cells** also are produced by the metamorphosis of myeloblasts. They are 25 to 30 μ in diameter and contain large multilocular nuclei that are often basket-shaped (Pl. 2, Fig. 6), with numerous central bodies and an oxyphilic, often fibrous protoplasm. Modern researches have made it probable that the blood platelets originate as divisional products of the bodies of these cells.

The development of the **fatty marrow** from the red takes place in such a way that the number of medullary cells gradually decreases, while the cells of the reticulum enlarge and fill the meshes. Minute drops of fat appear in the bodies of the enlarged cells, gradually coalesce into fat globules and displace the cellular elements that take part in the formation of the blood.

The **arteries of the bones** are divided into the superficial and the deep. The former enter the periosteum and form wide meshed plexuses in the adventitia, from which twigs pass everywhere through the fibroelastica and enter the compact bone substance in the Haversian canals, through which they run to anastomose with the deep vessels. The deep arteries, known as the nutrient, pass obliquely through the compact substance to the medullary cavity, where they break up into large capillaries that assemble again into veins with

very thin walls. The **veins** accompany the arteries and are generally two in number.

The **lymphatics** of the periosteum form a plexus that opens internally into an interspace between the periosteum and the bone, and is connected in the other direction with the interspaces of the bone marrow through the Haversian canals. All of these spaces are lined with epithelium, so that the blood vessels in the Haversian canals are surrounded by lymphatic sheaths.

The **nerves** of the periosteum are both medullated and nonmedullated. The former may end in Pacini's corpuscles. Exclusively nonmedullated nerves reach the interior of the bone along with the blood vessels, but are destined for the muscles of the latter. It is not probable that sensory fibers enter the bones.

4. THE JOINTS

The joints originate as clefts in the connective tissue surrounding the pieces of the skeleton, still cartilaginous at this time, which are at first peripheral and later press in between the ends, while the layer of connective tissue lying next to the cavity becomes differentiated into the capsule of the joint and is continuous with the perichondrium.

The **articular capsule** surrounding each joint is divided into an outer ***stratum fibrosum,*** and an inner ***stratum intimum,*** or ***synovial membrane.*** The stratum fibrosum blends with the periosteum of the ends of the bones that meet to form the joint, and consists of parallel bundles of connective tissue packed closely together, which have a rather circular course in the deep layers and a longitudinal one in the superficial. Sparse elastic fibers lie between the bundles. The **intima** originates from the cartilage covering the ends of the bones and forms folds and villi that project into the joint. It consists of loose connective tissue containing many stellate anastomosing fibroblasts, and forms a more or less coherent layer over the free surface.

The **articular surfaces** of the bones are usually covered with hyaline cartilage, which projects without any covering into the cavity of the joint and blends at its margin with the intima, with a great multiplication of cells that here become stellate. The sternoclavicular joint forms an exception, as this has a coat of fibrocartilage. The movements of the joint appear to wear away the surface of the cartilage with an unraveling of the fibers of its basal substance and a disintegration of its capsules. The cartilage capsules are flat and lie parallel to the surface in the superficial layers, but deeper in they are roundish and unite in the formation of territories, and still deeper they form the cartilage columns. The articular cartilage is separated from the bone by a layer of calcified cartilage.

A small quantity of yellowish, viscid fluid, the **synovia,** is always to be found in the cavity of the joint, containing the destroyed elements from the articular surface. Its reaction is alkaline, its chemical composition depends upon the condition of the joint as regards rest, because the amount of organic constituents is increased when the joint is in active motion. Among the organic constituents may be mentioned albuminoids and the synovial mucin.

The **intermediate discs,** or **menisci,** found in many joints, consist of fibrocartilage, as do also the **labia glenoidalia.**

The joints are abundantly supplied with **blood vessels,** which enter the intima and break up there into capillaries. The latter are also found in the villi and folds of the intima.

The **lymphatics** of the joint form plexuses in the stratum fibrosum and the stratum intimum. No connection seems to exist between them and the cavity of the joint.

The joint also has **medullated nerves** which enter the intima and form there a superficial plexus, from which fibers extend to terminate in ovoid end corpuscles.

5. THE SYNARTHROSES

In the synarthroses two bones are joined either by ligaments of connective or elastic tissue, **syndesmoses,** or by cartilage, **synchondroses.** The latter are found in the vertebral column, where the vertebræ are joined together by the intervertebral discs, or **fibrocartilagines intervertebrales,** each of which consists of an external, concentrically laminated **annulus fibrosus** of fibrocartilage and an internal **gelatinous nucleus,** the **nucleus pulposus.** The latter is composed of masses of vacuolized cells, the remains of the former chorda cells.

VIII. THE ORGANS OF THE NERVOUS SYSTEM

1. THE SPINAL CORD

The **neural crest,** running in the median line of the ectoderm, forms the matrix from which the spinal cord and brain develop. It hollows out to form the **neural groove,** and even at this stage an anterior ***brain portion*** and a posterior ***spinal cord portion*** may be recognized. The closure in of the neural groove to form the **neural canal** begins at the junction of the brain and spinal cord portions, and extends thence forward and backward, so that by the beginning of the fourth fetal week the entire neural canal is closed in. The **spinal cord** at this time is a quadrangular tube with a broad ventral and a narrow dorsal surface, through which passes longitudinally the wide **central canal,** lozenge-shaped on section and divided into right and left halves that unite dorsally and ventrally. The central canal is surrounded by an **ependymal layer,** outside of which is the cellular **mantle layer,** and quite externally each half is invested by the narrow **marginal film** consisting wholly of nerve fibers. The cells of the mantle layer, the development of which has already been discussed, are completely developed with their neurites and dendrites at this time.

The spinal cord now increases in size and assumes by degrees its definitive form. The size of the central canal is diminished by the approximation and fusion of the walls of its dorsal half, leaving only the ventral portion that is small, roundish, or oval on cross section. The ependymal cells form with their processes a septum separating the two dorsal halves of the medulla, the **septum posterius.** At the same time the ependymal layer becomes thinner, while the mantel layer, known now as the **gray matter,** becomes very thick and forms the main part of the medulla. The nerve cells are scattered uniformly through the gray matter at first, but later collect into quite definite groups. Beginning at the end of the second embryonal month the gray matter gradually assumes its typical form, hand in hand with the increased growth of the neurites into the **white matter,** the anterior horns appearing first, then the posterior. The first medullary sheaths appear in the roots in the fifth month, and the formation of medulla extends from here to the dorsal and ventral parts of the white matter, leaving the middle portions the longest without medulla.

We shall now glance over the gross structural relations of the spinal cord as shown in a section of the fourth cervical segment (Pl. 73, Fig. 167).

The section is bounded externally by a thin layer of neuroglia, known as the **glia capsule,** which sinks into a wedge-shaped fissure in the middle of the ventral surface, the **fissura longitudinalis anterior,** and covers its walls. It behaves similarly in the middle of the dorsal surface, although we can hardly say that there is a fissure at this place. The glia capsule sinks deeply into the substance of the spinal cord forming a thin, glial septum, the **septum longitudinale posterius.** Furthermore, numerous branching septa

extend into the spinal cord from the glia capsule; among these there is one on each side placed laterally from the posterior longitudinal septum and called the **septum paramedianum.**

The cross section of the spinal cord is imperfectly divided by the anterior fissure and the posterior longitudinal septum into two halves, a right and a left, which are connected by a central bridge. Each of these consists of a gray nucleus, the **gray matter,** and an enveloping white mantle, the **white matter,** which are thus named from their appearance in the fresh preparation. The white matter owes its color to the fact that it is composed almost exclusively of medullated nerve fibers. The gray matter has a smaller number of these and is mainly composed of nerve cells and nonmedullated fibers.

The two gray halves are connected by a transverse bridge, the **gray commissure,** which adjoins the white matter on its dorsal side, contains the **central canal,** and is separated on its ventral side from the bottom of the anterior fissure by a transverse ridge of medullated nerve fibers that connects the two white halves of the spinal cord, the **white commissure.** Dorsally from the central canal there also appear fine, transverse, medullated bundles, which together form the **posterior white commissure.**

In this section of the spinal cord the gray matter is shaped like a butterfly; in each half it swells ventrally into a hammer-shaped formation, the **anterior horn,** from the ventral surface of which the slender **anterior roots,** which are hard to see, radiate in little bundles to the periphery. Large nerve cells are found in the anterior horn arranged in groups that are known as the **anterior median, anterior lateral, posterior median, posterior lateral,** and **central.** Laterally a pointed process, the **lateral horn** with large nerve cells, is detached indistinctly from the anterior horn. Farther dorsally the gray matter is reduced considerably to form the **posterior horn,** which runs in the neighborhood of the periphery with a somewhat dorsal curve, and ends at the place where the **posterior roots** enter. Between the lateral and posterior horns, in the so-called lateral tract angle, the gray matter is dispersed by the reticulated fibers of the white matter into little islands to form the **processus reticularis.** We may distinguish in the posterior horn, the broad **intermediate zone,** the narrow **neck,** and the longitudinally oval **head.** The head is enveloped dorsally by a crescentic mass of gray matter, the **substantia gelatinosa Rolandi.** Peripherally to this is the reticulated **stratum zonale,** which is separated from the surface by a narrow layer of longitudinally running medullated fibers, the **stratum terminale,** or **Lissauer's tract.** The nerve cells in the posterior horn are small and can be seen only with difficulty.

The mantle of **white matter** is readily seen to be divided into three large territories on each side by the incoming and outgoing roots; the wedge-shaped **posterior column** between the septum longitudinale posterius and the posterior root, the **lateral column** between the posterior and the anterior roots, and the **anterior column** between the anterior root and the anterior fissure. In the posterior column the septum paramedianum incompletely separates the **column of Goll,** situated to its median side, from the laterally situated **column of Burdach.**

The grosser changes shown in sections of the spinal cord at different levels consist 1, in the form of the section as a whole; 2, in the form of the gray

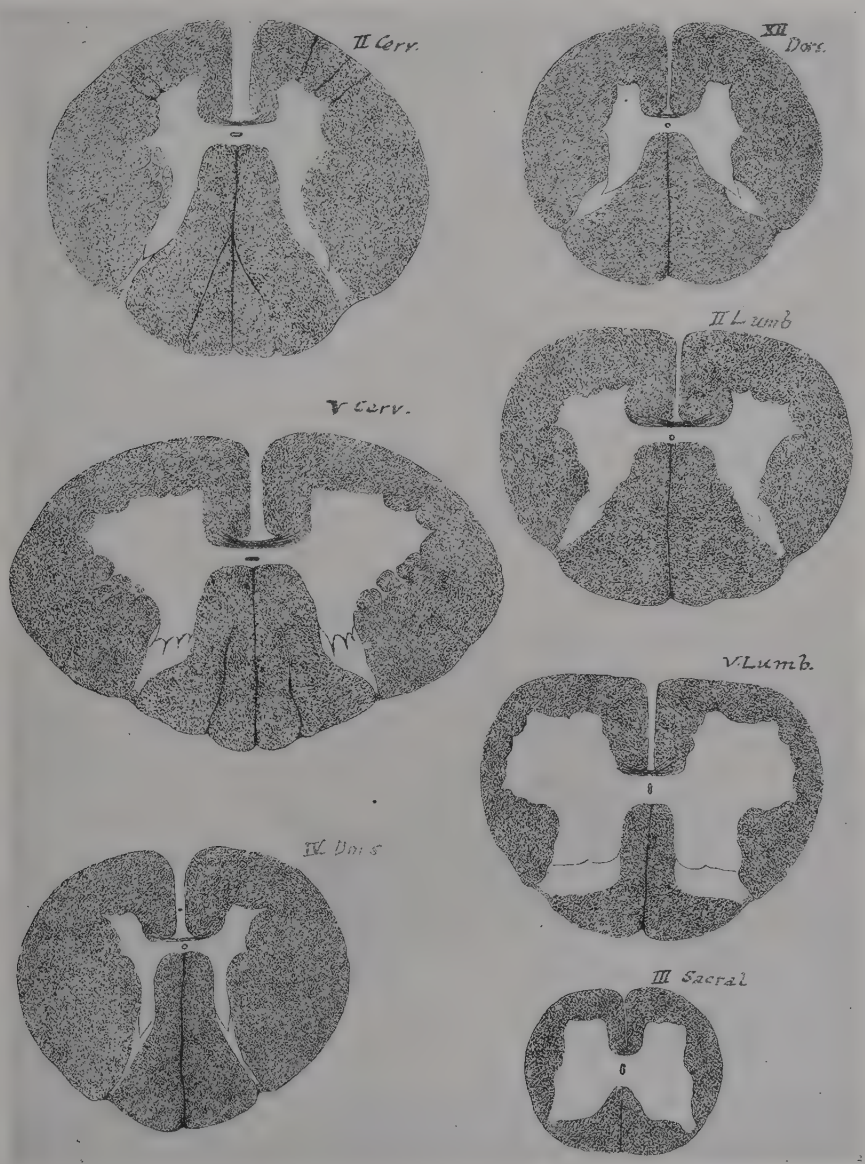


Fig. 35.—Shapes and Sections of the Spinal Cord at Various Levels.

matter; 3, in the relations between the gray and the white matter; 4, in the form of the central canal. The accompanying drawing will convey more information concerning all of these points than would an extensive description.

We shall now study more closely the minute structure of the gray matter.

a. The Gray Matter

The gray matter of the spinal cord is composed of ***nerve cells*** and ***fibers,*** aside from the neuroglia and blood vessels. Part of the fibers are neurites of the cells, part enter the gray from the white matter and terminate here.

The **nerve cells** form, as we have seen, five well distinguished groups in the anterior horn, but we always find scattered cells between these groups. Just as the anterior horns of the spinal cord form the **anterior columns** in the white matter, so these individual groups of cells form **cell columns,** but they differ from the former in not being continuous, as distinct interruptions, or **segmentations,** may be seen.

The **cells of the anterior horn** are multipolar nerve cells, and the very great majority of them have neurites that become surrounded by a medullary sheath sooner or later after they have left the cells. They may be divided into three large groups in accordance with the further course of these neurites, the **root cells,** the **commissural cells,** and the **columnar cells** (Pl. 79, Fig. 176).

The largest cells of the spinal cord are the **root cells,** measuring 150 μ, which always contain a vesicular nucleus and large Nissl bodies. They send out several strong ***dendrites,*** that pass through the gray matter for long distances and come into contact with other cells. The always single ***neurite*** extends from the cell body, or from a dendrite, then suddenly thickens, becomes clothed with a medullary sheath, and arches over to the ventral surface of the anterior horn, where it becomes an **anterior root fiber** (Pl. 81, Fig. 178). Just before its exit from the gray matter it gives off one or more ***collaterals*** to the neighboring cells. Each anterior root fiber is motor and runs without interruption from its root cell to the muscular fiber under its control, on which it ends in a motor end plate. Hence all of the root cells of the anterior horn are motor. The only exception to this rule is that certain cells may rarely be observed to send their neurites through the posterior horn into the posterior root.

While the root cells are distributed among all of the cell groups of the anterior horn, the **commissural cells** occur mainly in the median groups and extend from here into the anterior gray commissure. They are usually smaller than the root cells and of a more elongated form. Their ***neurites*** pass, after they have received their medullary sheaths, into the ***anterior white commissure,*** cross the middle line, and reach the ***anterior column*** of the opposite side, where each divides into an ascending and a descending branch. Thus a constant decussation of fibers takes place in the anterior commissure (Pl. 81, Fig. 178).

The **columnar cells** are those whose ***neurites*** run in the ***white matter*** of the same side. They are not confined to the anterior horn. They are of medium size, are found chiefly in the central groups, and are characterized by very strong and very long dendrites. The neurite of each divides, after it has been invested with medulla, often within the gray matter, into several branches, **schizaxons,** which usually enter the **lateral column,** less often the **anterior column** of the same side, and divide into ascending and descending fibers (Pl. 81, Fig. 178).

The **cells of the lateral horn** and of the **formatio reticularis** are of medium size and are all **columnar.** They send their neurites into the ***lateral column*** of the same side.

The **cells of the posterior horn** are generally smaller than those of the anterior and are not arranged in groups. They are at most of medium size and are unevenly distributed in the head and neck. Their **neurites** enter either the **lateral** or the **posterior columns** of the same side. Cells of **Golgi's second type,** which have already been described, are found with them very often.

A well differentiated group of cells is to be found only in the median portion of the base of the posterior horn; these are known as **Clarke's cells** and form the **column of Clarke,** which extends from the lower cervical down into the sacral medulla. Clarke's cells are large and have several thick, gnarled dendrites. The **neurites** assemble into bundles that are often very distinct, **Flechsig's bundles,** which pass transversely through the base of the posterior horn to enter the ***lateral column,*** in which they turn toward the brain (Pl. 79, Fig. 176).

The **substantia gelatinosa Rolandi** has a homogeneous basal substance produced by the degeneration of nerve cells during embryonal life, and contains in adults three kinds of nerve cells; small, scattered, ***stellate columnar cells,*** the neurites of which enter the posterior columns; elongated, ***pyramidal columnar cells,*** with their longitudinal axes in the axis of the posterior horn, the neurites of which enter the **posterior column,** and the so-called ***border cells,*** which are elongated and lie in the periphery of Rolando's substance with their longitudinal axes vertical or oblique to the axis of the posterior horn. Their **neurites** run through the latter longitudinally, then bend laterally and enter the **lateral column** of the same side (Pl. 79, Fig. 176).

If we turn now to the **nerve fibers of the gray matter** we shall note first that a part of them are **neurites** of cells situated here and as such leave the gray matter, while another part enter the gray from the white matter to terminate on the cells themselves with end arborizations. Consequently they are in part medullated, in part not. Each one of the former variety has a nonmedullated initial portion, each of the latter a nonmedullated end piece.

We have already learned to know the fibers that pass out of the gray matter as neurites of the root, commissural, and columnar cells. Those that enter the gray matter come, each and all, from the white, and are either end sections or **collaterals.** The fibers running in the white matter give off at right angles from place to place lateral branches, or collaterals, which enter the gray matter and end on its cells. We may divide them into the **collaterals of the anterior, lateral, and posterior columns** (Pl. 81, Fig. 178). Some enter alone, some in bundles; the latter are met with particularly in the posterior horn. They come from the posterior column, pass in parallel, finer or coarser bundles through the substantia gelatinosa Rolandi, or in a curved course through the median portion of the head of the posterior horn, and radiate partly to the cells of the posterior horn, partly to Clarke's, or else pass in compact lines through the cervix to enter the anterior and lateral horns and to end on their cells.

The **gray commissure,** which joins the two gray halves of the spinal cord, is divided by the central canal into a broad dorsal and a narrow ventral part, and consists mainly of **neuroglia.** We also find in it **dendrites** of the commissural cells, which pass from one half to the other, as well as **commissural cells** themselves, and medullated fibers. In the dorsal part the latter are in fact **collaterals** of the **posterior and lateral columns,** which unite into little bundles to pass over to the cells of the posterior horn of the opposite side. In the ventral part we have similar, but less strong collaterals coming from the anterior and lateral columns and passing through the commissure to the cells of the anterior, lateral, and posterior horns of the opposite side.

b. The White Matter

Aside from the glia, which will be described presently, the white matter consists of **medullated nerve fibers** running longitudinally and the **collaterals** that branch from them. The fibers vary much in caliber and have no sheaths of Schwann. The thickest ones are in the lateral column, the thinnest in the posterior. Various subdivisions may be made of this mass of fibers based partly on embryological, partly on experimental grounds, but it is difficult or impossible to distinguish them histologically. A brief description may enable us to understand better the extremely important relations in the organization of the spinal cord.

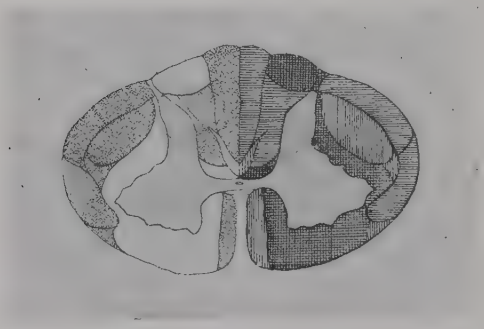


Fig. 36.—The Columns of the White Matter of the Spinal Cord at the Level of the Fifth Cervical Nerves.

In the right half of the figures the descending tracts are marked with vertical lines, the ascending with horizontal lines, those that both ascend and descend with crossbars. In the left half the long tracts are dark, the short are light. 1, pyramidal tract of the anterior column; 2, basal fasciculus of the anterior column; 3, Helweg's tract; 4, Gower's tract; 5, basal fasciculus of the lateral column; 6, Monakow's tract; 7, cerebellar tract of the lateral column; 8, pyramidal tract of the lateral column; 9, zona terminalis; 10, ventral bundle of Burdach's column; 11, Schultz's comma; 12, middle bundle of Burdach's column; 13, dorsal bundle of Burdach's column; 14, column of Goll.

The **anterior column** may be divided into two parts, the ***anterior pyramidal tract,*** and the ***basal fasciculus of the anterior column.*** The **anterior pyramidal tract** bounds the anterior longitudinal fissure on each side. It is best developed in the upper cervical portion, continuously decreases downward, and disappears in the dorsal portion of the spinal cord. This gradual disappearance is due to the fact that we have to deal here with a long **descending tract,** the fibers of which successively leave the column, pass through the anterior commissure, where they lose their medullary sheaths, and end on the cells of the opposite anterior horn. The **cells** from which the fibers **originate** lie in the **cerebral cortex.**

What remains after the anterior pyramidal tract has been deducted is known as the **basal fasciculus of the anterior column,** and in compari-

son with the other is **short,** containing fibers that originate in cells in the anterior horn. Each fiber divides like a T into an ascending and a descending branch, which send collaterals into the anterior horn and, after a longer or shorter course, bend at right angles and end the same as the collaterals.

The basal fasciculus of the anterior column passes over into the **basal fasciculus of the lateral column** in the region of the anterior roots. This does not reach the periphery in the cervical portion, diminishes in size downward, and contains, like that of the anterior column, **short tracts, neurites of the cells of the anterior** and **lateral horns.**

Externally to this, close dorsally to the place of exit of the anterior roots, we find in the cervical portion a little, triangular district of fibers, **Helweg's tract.** This is a **long descending tract,** the **cells of origin** of which lie in the **olivary bodies** of the medulla oblongata, while their fibers end in the cells of the anterior and lateral horns.

Dorsally the periphery of the lateral column is bounded by **Gower's tract,** likewise ***long,*** but ***ascending.*** Its fibers are the **neurites** of cells situated in the base of the **posterior horn.** They run upward in the gradually swelling tract to the medulla oblongata and finally to the cerebellum.

Still farther dorsally at the periphery of the spinal cord we meet with the important, **long, ascending, direct cerebellar tract,** which appears first in the upper lumbar portion, increases rapidly in strength, to become about constant in size in the lower cervical. By far the most of its fibers are the **neurites** of **Clarke's cells,** and they pass through the medulla oblongata to the cerebellum.

To the median side of the direct cerebellar tract lies in the cervical portion a large tract of fibers known as the **lateral pyramidal tract,** which may be followed caudally down into the sacral portion, decreasing much in size, especially in the cervical and lumbar swellings. The fibers of the lateral pyramidal tracts are ***long*** and ***descending;*** they originate from the cells of the **cerebral cortex,** undergo a **total decussation** at the junction of the brain and spinal cord, and are then gradually distributed to the root cells of the anterior horn, on which they break up into terminal arborizations.

At the place where the preceding adjoins Gower's tract the median part of the lateral column is occupied by the ***long, descending*** **Monakow's tract.** The cells of origin lie in the **red nucleus** of the midbrain, their neurites soon **decussate** and may be followed to the sacral portion, ending on the cells of the anterior horn.

The **posterior column** is divided into a median ***Goll's*** and a lateral ***Burdach's column.*** The **column of Goll** is wedge-shaped; its base is the dorsal periphery of the spinal cord from the septum longitudinale posterius to the septum paramedianum, from which it tapers ventrally and terminates in a point some way in front of the posterior commissure. It contains exclusively the slender ***fibers*** of the ***posterior root,*** which divide like a T, the ascending branches running in the column toward the brain. The number of fibers in the column of Goll constantly increases upward from the dorsal region, and they terminate in the medulla oblongata on the cells of **Goll's nucleus.** It thus contains the ***ascending portions of the posterior***

root fibers; the descending portions lie along the side of the column of Goll in the form of a slender, comma-shaped bundle, **Schultz's comma.** The descending portions are short and soon enter the gray matter.

Burdach's column has fibers that are thicker on an average than Goll's and includes all the rest of the posterior column. It is comprised likewise in great part of ***long tracts,*** especially in its **middle segments,** the ***ascending*** parts of the ***fibers of the posterior roots,*** which go to the medulla oblongata and end there in **Burdach's nucleus.** But it also contains many neurites of columnar cells of the posterior horn, which are short, and run chiefly on the peripheral base and on the opposite zone adjoining the posterior commissure.

c. The Anterior Roots

The fibers of the anterior roots are, as we have seen, the neurites of the root cells situated in the various groups in the anterior horn. They are invested with medulla at a greater or less distance from the cell, send out their motor collaterals and reach their bundles by a curved course. Each bundle contains fibers from different groups of cells (Pl. 81, Fig. 178). The bundles are quite slender and lie three or four together in the section of the spinal cord. They pass through the marginal district between the anterior and the lateral columns, at some distance apart are parallel, and converge from the so-called sulcus lateralis anterior to the anterior root (Pl. 83, Fig. 181).

Besides these root fibers the anterior roots contain a smaller number of others that originate from the root cells not of the same, but of the opposite side, come through the white commissure into the anterior horn and leave through the anterior root.

Finally, there are fibers of less caliber than those of the anterior roots, which originate in the cells of the lateral horn. These do not go to the striated muscle fibers, but enter the sympathetic ganglia, where we shall meet with them again.

d. The Posterior Roots

The conditions in the posterior roots are considerably more complicated. The medullated fibers that compose them vary a great deal in caliber and come from the **spinal ganglia.** The posterior root leaves the ganglion as a solid cord, soon divides into a considerable number of bundles which pass in the sulcus lateralis posterior to the median side of the posterior horn into the spinal cord (Pl. 83, Fig. 181). Four subdivisions of each posterior root bundle may be made from the subsequent course of the fibers. The most median subdivisions enter the posterior columns and become posterior column fibers, which have been described. Laterally from these are fibers that likewise enter the posterior column, but only pass through it in a curvilinear course to enter the posterior horn and to end on the cells of Clarke's column. Farther laterally are fibers that pass in parallel lines through the substantia gelatinosa to end on the cells of the anterior and lateral horns. The most median, finest fibers finally enter the stratum terminale to follow a longitudinal course and to end on the cells of the posterior horn.

Thus we see that the fibers of the posterior roots, in contrast with those of the anterior, are centripetal conductors; they come from the spinal ganglia, enter the spinal cord, and continue their courses within it.

e. The Neuroglia of the Spinal Cord and of the Central Canal

We have already studied the minute structure and the development of neuroglia and shall deal here only with its essential topographical relations. The spinal cord is surrounded by a **glia capsule** which varies in thickness from 2 to 20 μ, and is strongest at the dorsal and lumbar swellings. On the ventral surface it covers the walls of the anterior longitudinal fissure, while dorsally, together with other fibers, it forms the **septum longitudinale posterius.** It consists of strong, longitudinal glia fibers assembled into manifold bundles which here and there bend at right angles and enter the white matter. Part of the bundles of fibers turn outward to enter the surrounding pia.

Glia septa radiate into the white matter from the glia capsule, branch, become thin and for the most part break up before the gray matter is reached. These septa divide the white matter into larger and smaller districts, yet have little to do with the functional organization. They consist of glia fibers that radiate for the most part. The glia capsule is particularly well developed at the place of entrance of the posterior roots, where it surrounds the nerve fibers and penetrates with them into the spinal cord.

Glia fibers are to be found everywhere in the **white matter,** part running radially, winding between the nerve fibers, part longitudinally and parallel to the latter. Yet the mass of neuroglia between the fibers is by no means enough to permit us to say that it has an isolating function. Glia cells are also to be found everywhere between the fibers, containing their characteristically shaped nuclei that are rich in chromatin.

The **gray matter** also is abundantly supplied with neuroglia, which varies in different parts. It is densest about the central canal, which we shall study first (Pl. 80, Fig. 177). The **central canal** is lined with **ependymal cells** packed closely together, which are cylindrical in childhood and become more slender from the canal toward the periphery. Each cell is provided with a nucleus, cilia, and basal corpuscles. During youth the central canal begins to become obliterated from the sacral region upward, so that by middle life a lumen is usually to be found only in the upper cervical portion. The obliteration results from proliferation of the ependymal cells, which assume the character of astrocytes, such that the lumen is replaced by a mass of cells containing numerous glia fibers.

About the central canal there is a very dense and powerful accumulation of neuroglia, the **central mass of glia,** the fibers of which have a threefold course. The great mass of them are circular, with many longitudinal ones, frequently combined into bundles, passing between them. Other fibers, that follow a radiating course, are most strongly developed in the ventral and dorsal portions and form in each of these a glia cord from the central canal to the bottom of the anterior fissure, or radiating into the septum longitudinale posterius, the **ventral** and **dorsal ependymal wedges.** If these radiating fibers are traced toward the center they may often be seen to run to the ependy-

mal cells and to end in their protoplasm. The posterior longitudinal septum is therefore composed of fibers that are both ependymal, and from the glia capsule. The central mass of glia contains both glia cells and glia fibers, but the number of the former is in no true ratio to the enormous mass of the latter.

The relations of the glia fibers to the **blood vessels** may be observed very well in this region. A fairly thick mantle is formed about them, the **membrana perivascularis,** that is separated from the vessel wall by a narrow interspace that probably serves for the circulation of the lymph.

The **anterior horn** is always provided abundantly with glia fibers, which accompany the outgoing anterior roots and form a dense mass at the margin of the white matter. A basket of glia fibers is formed about each nerve cell. These **glia baskets** are not immediately contiguous to the bodies of the nerve cells, but the two are always separated by an interspace. In the **posterior horn** Clarke's columns are the richest in glia, while Rolando's substance is the poorest and contains only quite few glia fibers.

With regard to the **function of the neuroglia,** the part that has been ascribed to it, that of being a separating substance, can hardly be justified. Whether it is merely a filling in material, or is essentially important to the nutrition of the spinal cord, needs further elucidation.

f. The Blood Vessels of the Spinal Cord

The **arteries** that supply the spinal cord with blood come partly from the vertebral, partly from the paired segmental branches of the abdominal aorta and their caudal continuation in the median sacral, the lumbar, and the lateral sacral. From the vertebral artery comes the anterior spinal, at first paired, later unpaired, which runs downward ventrally from the anterior longitudinal fissure, and the paired posterior spinal descending along the dorsal surface of the cord. The spinal branches pass from the segmental vessels through the intervertebral foramina into the vertebral canal, and give off the ramuli medii on the cord. An arterial plexus about the spinal cord is produced by the formation of a chain of anastomoses between these separate tracts. Vertical twigs branch off here and there from the longitudinal vessels and the plexus just mentioned, to penetrate into the cord. The most important of these are the arteriæ sulci, about two hundred in number, which are given off from the anterior spinal, pass deeply into the anterior longitudinal fissure, then bend and enter alternately the right and the left halves of the spinal cord and the gray matter on each side of the central canal as the longitudinal central arteries. On the dorsal surface the arteriæ septi posteriores radiate into the posterior septum. Radiating branches from the plexus enter the entire periphery of the cord, but particularly with the anterior and posterior roots; these little vessels when taken together are commonly known as the vasocorona. All of these little arteries break up in the spinal cord into capillaries that form plexuses about the nerve fibers arranged longitudinally in the white matter. Denser capillary plexuses are also formed in the gray matter, especially in the region of the cells of the anterior horn and of Clarke's columns. While the capillaries of the gray matter come mainly from the arteriæ sulci, those of the white matter are derived chiefly from the vasocorona.

The **veins** of the spinal cord form three anastomosing longitudinal trunks on both the ventral and the dorsal surfaces, an anterior and a posterior median, with two anterior and posterior lateral veins running near the roots. The blood flows partly into the intervertebral veins, partly into the plexus venosi vertebralis interni. Within the spinal cord itself the veins generally follow the course of the arteries.

g. The Lymphatics of the Spinal Cord

The lymphatics of the spinal cord are unenclosed spaces about the blood vessels that are separated from their surroundings by the glial membranæ perivasculares. Enclosed lymphatics are totally wanting. These perivascular spaces within both the white and the gray matter are in open connection with a system of clefts between the nerve fibers and about the cells in which glia fibers run. They open into the subarachnoidal space.

2. THE SPINAL GANGLIA

The first sign of the spinal ganglia is met with very early, at the time when the neural plate is transformed into the neural tube. At the place where the transition of the neural tube into the ectoderm takes place, cells separate from the latter, penetrate between the neural tube and the myotome and form together a longitudinal ridge, the **ganglionic crest.** After this has separated from the ectoderm and from the now closing neural tube, it divides into segments, i.e., it breaks up into a number of successive cellular masses, each of which belongs to a primitive segment.

The cells composing the spinal ganglia are at first equivalent, but later differentiate in two directions. Part of them increase in size, develop neurofibrils within themselves that extend out of the cells in the form of two processes, and become **bipolar nerve cells.** The others remain small and surround the larger ones as **amphicytes,** or **mantle cells.**

One of the processes of the cell passes through the wall of the now closed neural tube and becomes a **posterior root fiber,** the other passes to the periphery as a **sensory nerve fiber.** The primitive bipolarity of the cells of the spinal ganglia is lost in man fairly early through the growth of the cell body perpendicularly to its longitudinal axis, so as to be first drawn out into a pedicle into which both processes open. The further longitudinal growth of this pedicle results finally in a **unipolar nerve cell,** the process of which bifurcates like a T into the two nerve fibers.

Each spinal ganglion in the adult is surrounded by a dense **capsule of connective tissue,** which usually contains fat cells and elastic fibers. The capsule sends processes into the substance of the ganglion which anastomose and surround groups of cells. The connective tissue of the capsule is continued over the posterior root on the one hand, and over the spinal nerves on the other.

The contents of the ganglion consist of **nerve cells** and **nerve fibers.** The former lie in nests and elongated complexes joined together by bundles of medullated nerve fibers (Pl. 83, Fig. 181). Each nerve cell is surrounded by a capsule of fine, interwoven connective tissue fibers with flat connective

tissue cells between them. Between the bodies of the nerve cells and the wall of the capsule lie a varying number of little cells, the **amphicytes** (Pl. 29, Fig. 74). These, as we have seen, have the same origin as the nerve cells and may either form a layer about the latter, or lie separately. They continue over the nerve fiber as it leaves the cell and form upon it the **sheath of Schwann.**

The **cells of the spinal ganglia** vary much in size and shape. Usually the cell body is spherical or ovoid (Pl. 83, Fig. 182). The nucleus is large, vesicular, and exhibits all of the well known characteristics of nuclei of nerve cells. The body of the cell contains very many, and usually quite fine Nissl bodies scattered about pretty uniformly. They are absent in only one place, that of the origin of the process. The great majority of the cells of the spinal ganglia have only one process and are therefore **unipolar.** This process is fairly strong, arises from a conical eminence, and soon after its origin is often thrown into numerous coils that either embrace the cell body, or form a **glomerulus** situated in a depression of the cell body. Then the process breaks through the capsule and bifurcates like a T. It is invested first with a sheath of Schwann as a direct continuation of the intracapsular amphicytes, and soon after by a medullary sheath. **Two medullated nerve fibers** thus arise from the process, one passing into the spinal cord as a **posterior root fiber,** the other to the periphery in the spinal nerves as a **sensory nerve fiber.**

It is by no means rare for the protoplasm of the nerve cell to show **holes** or **apertures** filled with amphicytes at the place of exit of the process, which may occupy a fairly large portion of the cell body.

In addition to the nerve process we find in many cells other similar formations, as little intracapsular **clubs,** or **buds,** or as **longer processes** that pass through the capsule and end in the neighborhood in a little clubbed thickening. This end club is always surrounded by a little, separate capsule.

The nerve fibers issuing from the ganglion unite with the ventral root coming from the spinal cord to form a **spinal nerve,** which is connected by a ramus communicans with a sympathetic ganglion. In this way numerous **non-medullated fibers** run backward into the spinal ganglia and reach many, but not all spinal ganglion cells. Such an **afferent fiber** passes through the capsule and either forms an extremely fine meshed intracapsular plexus about the cell, or attaches itself to the cell body as a convolution (Pl. 83, Fig. 182).

It has been determined by careful computation that the number of medullated fibers which enter in the posterior roots is materially less than that of the nerve cells in the ganglia, although the two should correspond according to what has been said. The explanation of this fact is that medullated fibers may also be seen to end within the ganglion with simple clubs. A certain part of the nerve cells of the ganglion also are still in a latent, embryonal condition, in which they send out no processes.

The **arteries** of the spinal ganglia come mainly from the rami spinales of the segmental branches of the aorta. They form dense capillary networks in the ganglia about the capsules of the cells and the nerve fibers.

Lymphatics seem to be totally absent.

3. THE BRAIN

Inasmuch as a description of the structure of the brain that was only approximately full and coherent would far exceed the limits of this book, we must confine ourselves here to a brief histological analysis of its most important parts, and refer the student to special textbooks on neurology for a more complete discussion.

a. The Nuclei of the Afterbrain and Midbrain

In the **medulla oblongata** the gray matter undergoes a great disruption and remodeling, so that it comes to surround the mass of white fibers, and forms the floor of the fourth ventricle from the opening of the central canal. In addition numerous masses of nerve cells or nuclei appear in the medulla oblongata, some of them interpolated as intermediate stations in the cerebrospinal conduction, some serving as centers of origin or of termination for the cranial nerves. We shall deal briefly with the most important of these.

The **accessory nucleus** is the first that we meet with. It appears in the central cervical portion as a group of cells situated dorsolaterally from the central cells of the anterior horn, which have the characteristics of root cells, except that instead of sending their neurites ventrally into the bundle in the anterior root they send them laterally and toward the cerebrum through the lateral column (Pl. 75, Fig. 170). Farther up the fibers run more horizontally and unite with those that rise from below into the **spinal accessory** nerve. Collaterals from the posterior columns and the pyramids terminate on the cells of the accessory nucleus. The nucleus is shoved toward the median line by the decussating pyramidal fibers and comes to lie just laterally from the central canal.

The **nuclei of the posterior columns** appear at the level of the decussation of the pyramids, first in the column of Goll, a little later in that of Burdach (Pl. 75, Fig. 171). The cells are multipolar, medium sized, with long dendrites that have many branches. The fibers of the posterior column end on these cells with arborizations, while from them come neurites which, taken together, form the lemniscus, which decussates soon after leaving the nucleus. This is called the **decussation of the pyramids.**

Before the nuclei of the posterior column have reached their greatest extent and are prominent externally as the clava and the tuberculum cuneatum, the anterior pyramidal tract has joined the lateral pyramidal tract, which passed through the decussation, to form the **pyramids,** on the ventral periphery of which is the **nucleus arcuatus.** This stretches for a variable distance toward the cerebrum, and consists of multipolar cells of different sizes which are intercalated in the course of the fibræ arcuatæ externæ (Pl. 76, Fig. 172).

Another motor nucleus appears ventrally from the accessory before the central canal has opened; this is the **hypoglossal nucleus,** which appears later in the calamus scriptorius on the floor of the fourth ventricle (Pl. 75, Fig. 171; Pl. 76, Fig. 172). The cells resemble exactly the large root cells of the anterior horn, and their dense neurites form the root of the hypoglossus,

which leaves the medulla in a ventro-lateral direction, dorsally from the pyramid. Fibers that come from the cerebral cortex and decussate in the raphe end in the nucleus, as well as collaterals from the intramedullary course of the trigeminal, glossopharyngeal, and vagus nerves.

At the caudal beginning of the hypoglossal nucleus appears a formation that gives a cross section of the medulla oblongata its characteristic mark, the **lower,** or **large olive,** or **olivary body,** the **nucleus olivaris inferior** (Pl. 76, Fig. 172). This is a many folded double lamella of gray matter that opens medially, is closed laterally, and occupies the region dorsal to the pyramids. The entering nerve fibers form a medullary substance between the two lamellæ, while the latter become bordered by medullated fibers, the **stratum zonale.** The nerve cells that compose the nucleus are small, or at most of medium size, spindle-shaped, have several dendrites and one neurite each, which pass to the raphe, turn to the opposite side, and pass through the olive to appear in the corpus restiforme as the **fibræ arcuatæ internæ,** or the **tractus olivo-cerebellaris.** Fibers also pass from the vertex of the olive into the spinal cord, where we have met with them in the lateral column as **Helveg's tract.** Collaterals from the fibers of the direct cerebellur tracts, and fibers coming from the thalamus end on the cells of the olive.

Besides the large olive we meet with the **median accessory olivary nucleus** a little earlier, and **dorsal accessory olivary nucleus** rather later. These have essentially the same structure and the same connections as the large olive.

Medially from the olive toward the dorsum lies the **substantia reticularis,** passed through in the median line by the raphe. This contains many medium sized and large multipolar nerve cells, the axis cylinders of which turn toward either the brain or the spinal cord and are united into little bundles. Fibers coming from the cerebellum end on these cells.

In the dorsolateral parts of the formatio reticularis are large, multipolar cells that form the vagoglossopharyngeal nucleus, or the **nucleus ambiguus.** The neurites of these are hard to see because they always run singly; they join the vagoglossopharyngeal root, which will be mentioned later (Pl. 76, Fig. 172).

The principal nucleus of these nerves is the **vagoglossopharyngeal,** which occupies the region of the ala cinerea. It consists of several groups of medium sized cells with few dendrites and slender neurites, which leave the medulla oblongata together with the fibers from the nucleus just described.

Finally we have a third, the sensory **vagoglossopharyngeal nucleus,** which is a thin band of medium sized cells situated laterally and somewhat ventrally from the foregoing, and extending caudally to the level of the decussation of the pyramids. The fibers coming from the ganglion of the vagus and glossopharyngeal nerves enter the cerebral end of this nucleus and turn toward the cauda, forming a roundish bundle known as the **tractus solitarius** situated medially from the nucleus. The fibers end on the cells of the nucleus (Pl. 76, Fig. 172).

Somewhat higher we come to the region of the nucleus of the **auditory nerve** (Pl. 76, Fig. 172; Pl. 77, Fig. 173). As is well known this nerve enters the medulla oblongata in two roots, the fibers of which are the neurites of the

ganglia situated in the internal ear. The fibers of the lateral **root of the auditory nerve** come from the spinal ganglia of the cochlea and enter the **ventral nucleus,** which is situated between the cerebellum and the corpus restiforme. This nucleus consists of roundish or polyhedral cells with several dendrites and one neurite. The fibers of the lateral root end on them, some with special cup-shaped end organs. The neurites of the cells take different courses; part of them pass as the **striæ medullares** to the floor of the fourth ventricle and through the raphe to the upper olive, or to the lateral lemniscus. Another part forms the trapezium cerebri that will be described later.

Another nucleus of the lateral root of the auditory nerve is the **tuberculum acusticum,** which is situated dorsally from the ventral nucleus, and is very feebly developed in man. It is composed of multipolar, elongated cells adjoining the dorsal surface of the restiform body, the neurites of which run together with those of the ventral nucleus in the striæ medullares.

The **median root of the auditory nerve** is composed of neurites of the ganglion vestibulare, situated in the internal auditory meatus, and enters various nuclei. The first to be mentioned is the extensive **dorsal nucleus of the auditory nerve,** that lies in the floor of the fourth ventricle. This consists of cells of various sizes on which the root fibers end, the neurites of which decussate in the raphe to then pass toward the brain and into the tegmentum.

Another part of the median root of the auditory nerve enters **Deiter's nucleus,** bends about caudally and ends on the cells of this nucleus. The fibers are collected into little bundles, which give the nucleus its characteristic appearance. It lies laterally from the median nucleus of the auditory nerve and is composed of multipolar cells that differ greatly in size. Their neurites take different courses. Those from the more cerebral parts form the **tractus vestibulo-cerebellaris,** and enter the cerebellum through the cerebellar peduncle to end in its nuclei. The more caudal cells on the contrary send their neurites caudally and thus form a **tractus vestibulo-spinalis,** which runs in the lateral column and may be demonstrated as far down as the lumbar portion of the cord.

Still more laterally, on the medial periphery of the restiform body that is now radiating into the cerebellum, is **Bechterew's nucleus,** which reaches up into the roof of the ventricle. A final portion of the median root of the auditory nerve enters this. Part of the neurites of its cells enter the tractus vestibulo-cerebellaris, part cross the root fibers, pass through Deiter's nucleus, and enter the **fasciculus longitudinalis medialis** ventrally from the dorsal nucleus of the auditory nerve to rise in it into the midbrain, and to end on the cells of the nuclei of the ocular muscles. Numerous neurites from Deiter's nucleus take the same course.

The **upper olive** appears after the lower one has disappeared and lies in the same situation. It forms, as we have seen above, an important terminal center for the striæ medullares, the fibers of which approach its cells. The latter are of medium size, spindle-shaped, send their neurites into the lateral lemniscus, and reach with them to the posterior corpora quadrigemina and the internal corpus geniculatum (Pl. 77, Fig. 173).

Just to the median side of the upper olive lies the **nucleus trapezoides,**

which is developed much better in animals than in man. It is enclosed in the mass of fibers that comes down from the ventral auditory nucleus and as a whole is known as the trapezium cerebri. The cells of the trapezoid nucleus are large and round, their neurites cross the raphe and pass with the lateral lemniscus of the opposite side to the medial corpus geniculatum. The approaching fibers split and embrace the cell body, as the hand clasps a ball.

The **facial nucleus** appears as the lower olive disappears, and lies laterally and dorsally from it, separated by Monakow's and Gower's tracts from the surface of the medulla oblongata. Cerebrally it has only a slight extent and consists of large, multipolar nerve cells, the neurites of which are the root fibers of the nerve. They unite into a strong bundle that passes in a dorsomedial and somewhat cerebral course to the floor of the fourth ventricle close to the median line, then suddenly turns at a right angle and runs 5 mm toward the cerebrum, bends again laterally and takes a ventrolateral direction, but which leads at the same time so far caudally that the exit of the nerve lies at the same level as the nucleus. This entire tract is known as the **inner genu of the facial nerve** (Pl. 77, Fig. 173). Fibers coming from the cerebral cortex radiate into the facial nucleus from the pyramids.

Dorsally from the facial nucleus lie groups of multipolar cells, the neurites of which come to light between the facialis and the acusticus and form the **portio intermedia Wrisbergi.** It also contains sensory fibers that arise from the cells of the ganglion geniculi, enter with the motor fibers into the medulla oblongata, pass over into the tractus solitarius and end on its cells.

The **abducens nucleus,** within the genu of the facial nerve on the floor of the fourth ventricle, is likewise made up of large, multipolar cells of the motor type. Their neurites collect into slender bundles, which take a ventrolateral course, first through the substantia reticularis, then the corpus trapezoides, and finally the pons, laterally from the pyramid, and make an exit. Fibers from the pyramids and collaterals of the fasciculus longitudinalis medialis enter and end in the nucleus.

We must now discuss briefly the relations of the origins of the **trigeminus,** of which there are four terminal nuclei and the same number of roots. The ***sensory trigeminal nucleus*** begins as the facial nucleus disappears, lying farther ventrally, nearer the floor of the fourth ventricle (Pl. 77, Fig. 173). It is composed of little multipolar cells on which a part of the fibers of the sensory trigeminal root coming from the Gasserian ganglion end, though the greater part of the latter bend down at right angles to form a nerve tract running far caudally into the spinal cord, the ***spinal root of the trigeminus.*** On it lies a mass that forms the direct caudal continuation of the sensory nucleus of the trigeminus and is composed of similar cells. The fibers of the spinal root end on the cells of this spinal nucleus of the trigeminus. If we follow this root toward the cauda we find it at first to the lateral side of the facial nucleus, then ventral to the corpus restiforme, dorsal and somewhat lateral from the lower olive, and passed through at this place by the median root of the acusticus, and by the fibers of the glossopharyngeus and vagus. Later the cellular mass lying medially from the root lightens up very much and finally passes into the substantia gelatinosa Rolandi of the posterior horn.

The fibers of the trigeminus may be traced down into the region of the second cervical nerves.

The third nucleus of the trigeminus is ***motor,*** lies medially from the sensory, and is composed of large multipolar cells, the neurites of which form the motor root of the trigeminus.

The fourth and last nucleus of this nerve is composed of large, roundish or ovoid, unipolar cells that are situated in the midbrain, laterally from the aqueduct, on the outer margin of the central gray matter. The cells are fairly separate and are frequently arranged in rows. The large cell process soon receives a medullary sheath and the individual fibers come together so that soon they form a fibrous cord, the ***mesencephalic root of the trigeminus,*** which adjoins the cells on the medial side. The farther caudally it goes, the more it turns ventrally until it finally unites with the motor root. It has not yet been determined with certainty whether we have to deal here with a motor root, or whether the cells are to be looked upon as sensory cerebral ganglion cells remaining in the central organ.

The **nuclei of the pons varolii** form masses of medium sized multipolar cells scattered about between the fibers of the pons. These fibers, which come down from the cerebrum, end on them, and the nearby pyramids send numerous collaterals to them. The neurites coming from these nuclei form as a whole the brachium pontis, which radiates into the cerebellum (Pl. 77, Fig. 173).

b. The Cortex of the Cerebellum

A white **medullary ridge** and a **gray cortex** may be differentiated even macroscopically in the cross section of every cerebellar convolution. The medullary ridge, or lamina medullaris, is made up of medullated nerve fibers which either leave the cortex as the neurites of its cells, or come from cells outside of the cortex and enter it to end on its cells (Pl. 78, Fig. 174).

The line of demarcation between the medulla and the cortex is not very sharp. The fibers of the medulla radiate in parallel lines into the cortex to form a plexus in about its middle, beyond which only a few pass externally. Three layers may readily be distinguished in the cortex. Next outward from the medulla is the ***granular layer,*** the ***stratum granulosum,*** which is very broad at the top of the convolution, but more narrow in the deeper part. On the outer surface of this is the ***stratum gangliosum,*** a single layer of large nerve cells that send their dendrites into the ***molecular layer,*** or ***stratum cinereum,*** which is of even thickness everywhere and bounds the cerebellar cortex externally (Pl. 81, Fig. 179).

The **granular layer** is characterized by **little,** very densely packed **granular cells,** of which only the nuclei are to be seen when ordinary methods of staining are employed. They are roundish or angular cells measuring at most 10 μ, that send out from three to five short, tortuous dendrites, which split up into several clawlike terminal branches. The dendrite grasps with each terminal claw the body of a neighboring granular cell. The slender neurite passes vertically toward the surface into the molecular layer, without receiving a medullary sheath, where it divides like a T. Both branches take a course

parallel to the surface and are known here as parallel fibers. We know nothing more about them.

Between the little granular cells are scattered the **large granular cells,** measuring up to 40 μ, which usually have rather elongated cell bodies and very many, much branched dendrites. The very slender neurite splits soon after leaving the cell, within the granular layer, into very minute fibrils, hence we have here cells of Golgi's second type.

The cells of the **stratum gangliosum** we have already become acquainted with as **Purkinje's cells.** They have large pyriform bodies, measuring 70 by 40 μ, the bases of which rest on the granular layer. One or often two dendrites extend from these into the molecular layer, branch in a plane vertical to the convolution, and form a very characteristic ramification through the entire thickness of the layer. If the section is made parallel to the course of the convolution the tree thus formed may be seen as a relatively small formation measuring 50 to 60 μ. The cell body presents, especially in its basal portion, well developed, coarse Nissl's clods, and encloses a vesicular, large nucleus with a large nucleolus. The neurite comes from the base of the cell, passes through the granular layer, receives a medullary sheath, and leaves the convolution through the medullary layer.

The most important cells of the **molecular layer** are the **basket cells.** These range in size from small to medium, are multipolar, and are found chiefly in the deeper layers. Their dendrites branch in the molecular layer, their neurites become medullated fibers which run vertically to the direction of the convolution and parallel to its surface, just above the stratum gangliosum, and give off here and there a collateral at a right angle to a Purkinje's cell, where it forms a terminal basket that closely grasps the body of each cell.

It follows from this description that the **centrifugal fibers** which pass out from the cortex of the cerebellum are the neurites of Purkinje's cells. They all terminate on the cells of the nuclei of the cerebellum, which are yet to be described.

The **centripetal fibers** that enter the cortex of the cerebellum come partly from the spinal cord, the direct cerebellar tract, partly from the medulla oblongata, the olivo-cerebellar, and the vestibulo-cerebellar tracts, partly from the nuclei in the pons, the ponto-cerebellar tract.

Numerous medullated fibers pass through the granular layer from the medullary layer to the cerebellar cortex to form a dense superficial plexus on the inner surface of the stratum gangliosum, from which in turn proceed fibers that for the most part soon lose their medulla in the molecular layer. In addition many so-called **moss fibers** split up into twigs that end between the cells of the granular layer. A final sort of centripetal medullary fibers are known as the **climbing,** which, after they have passed through the granular layer, climb up on the bodies and processes of Purkinje's cells, making manifold loops about them.

The **neuroglia of the cortex of the cerebellum** is fairly well developed and is represented chiefly by cells lying between and beneath those of Purkinje. Their bodies contain a lipoid, their processes and fibers radiate vertically to the surface to end here in footlike expansions. As all these feet

adjoin they form a **membrana limitans** over the outer surface of the cerebellum. The glia fibers coming from ordinary astrocytes are mainly vertical, with a few parallel to the surface.

The cerebellar cortex receives its **arteries** from the two cerebelli inferiores and the cerebelli superior, the branches of which enter between the convolutions and into the latter, where they form a dense capillary plexus in the stratum gangliosum and in the granular layer. The capillary meshes run longitudinally in the medulla, corresponding to the course of the fibers. The **venous blood** is carried away by the inferior and superior cerebellar veins.

c. The Nuclei of the Cerebellum

The cortex of the cerebellum contains several gray masses, the most important of which are the ***corpus dentatum*** and the ***nucleus tecti.***

The **corpus dentatum** strikingly resembles the lower olive in its configuration, and like it is a many folded lamina of gray matter with a median hilum. The medially placed gray masses of the **nucleus globosus** and of the **embolus** are nothing else than broken off portions of the corpus dentatum. The cells are multipolar. The fibers that enter the nucleus are those already known to us as the neurites of Purkinje's cells, together with others coming from the olive; they form very dense terminal baskets about the cells. A neurite originates from each cell, runs as a medullated fiber in the cerebellar peduncle to the red nucleus, and takes part in the formation of the **tractus cerebelli tegmentalis mesencephali.**

The **nucleus tecti** lies in the vermiform process just above the roof of the ventricle, and consists of materially larger cells than those of the corpus dentatum. These cells are spherical and contain a yellow pigment. Their neurites enter the medulla oblongata, form the **tractus fastigio-bulbaris,** and extend to the cells of the substantia reticularis as the **fibræ arcuatæ internæ.**

d. The Nuclei of the Midbrain and Interbrain

The **nucleus of the trochlearis** lies close to the middle line beneath the floor of the aqueduct at the level of the inferior corpora quadrigemina. The cells of which it is composed are of medium size and multipolar, their neurites leave the nucleus as the root fibers of the nerve, take a curved course laterally and cerebrally, bend toward the median line in the roof of the aqueduct, and finally reach the velum medullare anterius. Here they decussate with those of the other side and run laterally. Many fibers that come chiefly from the fasciculus longitudinalis medialis end on the cells of the nucleus.

The nuclei of the **oculomotor nerve** form the direct cerebral continuation of the preceding, and therefore lie in the region of the anterior corpora quadrigemina, ventrally from the floor of the aqueduct, and dorsally from the median longitudinal fasciculus. They are commonly known as the **lateral,** the **median,** and the **Westphal-Edinger nuclei,** which may be broken up into large celled and small celled subgroups. We find strikingly small, and medium sized to large multipolar cells, which are also to be differentiated by the thickness of their neurites, that pass through the fasciculus longitudinalis

medialis, enter the trigonum interpedunculare, and suffer a partial decussation. The decussating fibers come chiefly from the lateral nucleus.

The **posterior corpus quadrigeminum** consists of an oval gray mass, its **nucleus** enveloped by a **mass of medullated fibers,** the **stratum zonale.** The nucleus contains numerous nerve cells of various sizes, among which are many of Golgi's second type. The neurites of the rest of the cells leave the nucleus, turn medially and ventrally, and, after crossing in **Meynert's decussation,** run as the **tractus tecto-spinalis,** ventrally from the fasciculus longitudinalis medialis in the medulla oblongata and the upper part of the cervical portion of the spinal cord. The stratum zonale arises through the splitting of the lateral lemniscus caudoventrally on the posterior corpus quadrigeminum, so as to embrace it chiefly on the lateral side, and to send its fibers into the nucleus, where they terminate on the cells of the latter. These fibers come principally from the upper olive, from the nucleus of the lateral lemniscus situated laterally from this, and from the striæ medullares, and therefore represent the **tractus acustico-tectalis,** a part of the cerebral auditory tract from the lateral auditory root.

The **anterior corpus quadrigeminum** has on the other hand important relations to the **visual tract.** Four different zones may be seen on cross section. Most externally is a **layer of medullated nerve fibers;** beneath this is a broad layer of gray matter, the **stratum cinereum,** consisting of little multipolar nerve cells on which the fibers just mentioned end. Then follows a layer of larger cells and medullated fibers, the **stratum opticum** the cells of which belong for the most part to Golgi's second type. The medullated fibers that end on them are fibers of the **optic tract** which arrive through the superior peduncle. The fourth and last layer, the **inferior lemniscus,** also contain multipolar cells and medullated fibers. The latter are what remain of the fibers of the **lateral lemniscus,** the most of which end in the posterior corpus quadrigeminum as we have seen. To these are to be added a part of the **middle lemniscus,** which brings fibers from the nuclei of the posterior columns and sensory fibers from the trigeminus. Finally here also run neurites from the cells of the anterior corpus quadrigeminum, part of which reach the tractus tecto-spinalis through the above mentioned Meynert's decussation, while part pass through the peduncle of the anterior corpus quadrigeminum to the cortex of the occipital brain.

The **red nucleus** lies on each side of the middle line ventrally from the aqueduct and the fasciculus longitudinalis medialis. It is, as we have seen passed through by the root fibers of the oculomotorius and forms the terminal center for the neurites of the cells of the corpus dentatum of the cerebellum, but in addition it receives a large tract of fibers from the cortex of the forebrain, which end here on little multipolar nerve cells. Together with the latter are a much smaller number of large multipolar nerve cells, the neurites of which form the **tractus rubro-spinalis,** that decussates very soon, runs down dorsolaterally from the lemniscus into the spinal cord, where we have learned to know it as **Monakow's bundle** in the lateral column.

The **corpora geniculata** are connected with two different tracts. A part of the fibers of the **optic nerve** terminate in the **lateral corpus geni-**

culatum, while the **median** one is connected with the **auditory nerve.** The **lateral corpus geniculatum** consists of varying layers of **gray matter** and **medullated nerve fibers.** The former contains large and small, usually triangular nerve cells on which the optic fibers split up into terminal arborizations. All of the optic fibers do not end here, but a part of them enter the thalamus, and yet another part pass into the anterior corpus quadrigeminum. The neurites from the cells of the lateral corpus geniculatum pass through the fasciculus longitudinalis inferior to the **cortical visual center,** situated in the cortex of the occipital lobe.

The **median corpus geniculatum,** placed close to the preceding, is composed of medium sized, multipolar nerve cells, the neurites of which run to the **temporal lobes.** The fibers of the **lateral lemniscus** that do not enter the posterior corpus quadrigeminum terminate on them, and a part of the **optic fibers** enter the nucleus.

Quite a number of separate nuclei may be seen in the **thalamus opticus,** covered by the central gray matter, but will not be described here. They are separated by laminæ of medullated nerve fibers that form the upper surface of the **stratum zonale,** and are separated laterally from the internal capsule by the **latticed layer.** The cells of the nuclei are of medium size, multipolar, and have either long radiating, or short fasciculate dendrites. The former are called **stellate,** the latter **bush cells.** On the cells of the thalamus end **sensory fibers of the cranial nerves, fibers from the lemniscus,** fibers from the **red nucleus,** and particularly fibers coming from the **cerebral cortex** and known as a whole as the **corona radiata.** The neurites of the cells that compose the various nuclei leave the thalamus in like manner to go to the **cortex of the cerebrum.**

e. The Hypophysis

The **hypophysis,** or **pituitary gland,** has a double origin. Its anterior principal portion is a derivative of the epidermis and appears in embryos about 3 mm long as a pouchlike diverticulum of the epithelium of the primitive stomodæum, the so-called **Rathke's pouch.** A little epithelial vesicle is formed by the dilatation of its distal end, which for some time remains connected with the cavity of the mouth by a duct lined with epithelium. After the appearance of the cartilaginous base of the skull this duct disappears. The vesicle settles on the base of the interbrain and becomes metamorphosed through proliferation of its epithelium into a massive, cellular body with two lateral horns, the cells of which are arranged in much twisted trabecula. The second, subordinate part of the hypophysis is derived from the **floor of the interbrain,** where a diverticulum of the third ventricle is formed somewhat later than Rathke's pouch, the infundibulum. From the distal end of this a solid cone extends, approximates the posterior wall of the hypophyseal sac, and is embraced between the two horns. This forms the ***little posterior lobe,*** the other the **large anterior lobe** of the organ. The anterior and posterior lobes are separated in youth by a narrow, cleftlike space, which is what remains of the former cavity of the hypophyseal sac. It is lined with ciliated epithelium and disappears at the same time of puberty.

The **anterior lobe** of the hypophysis is covered by a **connective tissue capsule,** which appertains to the dura and continues over the posterior lobe. Connective tissue from this capsule enters the lobes with the blood vessels and sends out fine fibers that embrace the **cellular trabecula.** The **cells** lie close together in the trabecula and are of two different kinds (Pl. 41, Fig. 102). The majority of them are characterized by the fact that they contain numerous granules which stain intensively with acid dyes, and they are consequently called ***chromophilic cells.*** The others have bodies that take only a little stain and are therefore ***chromophobic cells.*** But it is quite probable that these two varieties are only cells in different stages of secretion. During pregnancy the organ is considerably enlarged, chiefly because of a multiplication of the chromophobic cells.

In the posterior part of the anterior lobe many **cavities** appear between the cells, which are arranged about them like epithelium. The cavity itself is filled with **colloid,** so that the organ has a marked resemblance to the follicles of the thyroid gland. Farther back, in the former cavity of the hypophyseal vesicle, vesicular and cystic formations are met with which do not contain colloid. This part of the parenchyma interpolated between the anterior and posterior lobes is also known as the **pars intermedia.**

The smaller **posterior lobe** of the hypophysis, which has also been named, on account of its derivation, the **neurohypophysis,** has scarcely any cells. It consists of connective tissue and neuroglia, and contains brown pigmented granules in the meshes of the connective tissue.

The anterior lobe of the hypophysis is a gland that elaborates an internal secretion which is of great importance to the growth of the skeleton. Growth is greatly inhibited when it is removed. A pathological enlargement of the anterior lobe causes an abnormal development of the hands and feet, as well as of the soft parts and bones of the face, producing the condition known as acromegaly. The hypophysis also secretes **pituitrin,** which acts to increase the blood pressure.

The **arteries** of the hypophysis come from the internal carotid and the circulus arteriosus, and form in the anterior lobe a very rich, sinusoidal capillary plexus closely adjoining the cellular trabecula. The blood vessels are very sparse in the posterior lobe. The **veins** empty into the cavernous sinus.

The **nerves** of the hypophysis are from two different sources. Some enter the posterior lobe as neurites of nerve cells situated in the wall of the infundibulum, pass through it and reach the anterior lobe. There are also many sympathetic fibers from the plexus of the pia in the anterior lobe. The nerves form plexuses in the latter about all sides of the cellular trabecula.

f. The Epiphysis

Three successive diverticula are to be found in the human embryo in the roof of the interbrain, the pineal cushion, the parietal vesicle, and the epiphysis. While the first two undergo complete involution, the epiphysis, which is at first vesicular, becomes a solid body through proliferation of its epithelium, and is connected with the stria medullaris through the habenula.

The **epiphysis** is enclosed in a **connective tissue capsule** that sends

numerous anastomosing septa into the organ, which divide the parenchyma into larger and smaller **lobules.** Within these septa are found neuroglia fibers and cells together with connective tissue fibers. Each lobule is composed of densely packed **cells,** the bodies of which contain granulations that stain. Still other neuroglia cells are interposed between these glandular cells, and certain branched ones have been described and pointed out as nerve cells. After the epiphysis has reached the acme of its development, in about the seventeenth year of life, signs of involution appear, just as in the thymus, which manifest themselves first by the appearance of spherical bodies in the nuclei of the cells. The connective tissue increases at the cost of the parenchyma, and lime salts are deposited in the parenchymatous cells, forming the so-called **brain sand,** little concretions of lime in which a very distinct concentric lamination may be seen.

Little is known as yet concerning the function of the epiphysis, but very recent clinical and experimental observations indicate that it is an organ that elaborates an internal secretion which exerts an influence over the development of the germinal glands and the secondary sexual characteristics.

The epiphysis is abundantly supplied with **blood vessels,** which come from the tela choroidea superior and form capillary loops about the cells. A yellow brown pigment is deposited in their vicinity.

The epiphysis also contains numerous **nerve fibers** that enter the organ with the blood vessels and form plexuses.

g. The Cerebral Cortex

Although the structure of the cortex of the cerebellum is quite uniform in all of its parts, that of the cortex of the cerebrum varies a great deal in different parts of the hemisphere, producing many modifications that cannot be taken into account here.

The cerebral cortex has a maximum thickness of 5 mm, and blends internally with the **medullary substance,** from which it is not separated by a sharply defined line (Pl. 78, Fig. 175). Six layers of the cells composing the cortex are commonly differentiated from their arrangement and structure. Most externally is the **molecular layer** composed of little nerve cells together with many glia cells. Among the former are the so-called **Cajal's cells,** slender, spindle-shaped formations that have their longitudinal axes placed parallel to the surface and send their processes in the same direction (Pl. 82, Fig. 180). These cells, which are particularly numerous in the embryonal cortex, seem to have no neurites. The **second layer** is that of the **small pyramidal cells,** which are small, measuring only 10 μ, and do not always have a typical pyramidal form, but may be polyhedral, or spindle-shaped. They lie very close together, and the deeper we go the larger they become, and the more they assume the typical pyramidal shape. We may thus distinguish a **layer of medium sized,** and then a layer of **large pyramidal cells** beneath the layer of small ones, the domain of which reaches beyond the middle of the cortex. These cells are conical, with their bases toward the medulla, their apices pointing toward the surface, and they are of all possible sizes up to 100 μ long and 30 to 40 μ in diameter at the base. The cell body is pro-

longed toward the cortex into the process at the apex, which, after giving off lateral twigs horizontally, breaks up in the molecular layer into several branches running perpendicularly to the surface. These branches bend suddenly at a right angle in the most superficial portion of the molecular layer, run parallel to the surface, and gradually become lost. Numerous lateral dendrites pass out from the entire body of the pyramidal cell, bifurcate continuously, and become lost in the neighborhood; those coming from the base are particularly strong. The neurite arises from the base, takes a straight course toward the medulla, is invested with a medullary sheath soon after it leaves the cell, and enters the medulla as a medullated, centrifugal fiber giving off numerous collaterals on the way. Between the pyramidal cells are many of **Golgi's second type,** which are especially common in the region of the small pyramids. Next to the large pyramids comes the **granular layer.** Here we have exclusively little polyhedral cells, the neurites of which behave the same as those of the pyramidal cells. The following layer is characterized by very large pyramidal cells, and is known as the **layer of giant pyramidal cells,** or as the **ganglion cell layer.** Sixth and last is the **spindle cell layer,** where we find polyhedral and spindle-shaped cells with neurites passing into the medulla, and also little, polyhedral, Martinotti's cells, the neurites of which pass up into the molecular layer to become **tangential fibers.**

The outermost layer of the cortex is quite free from **medullated fibers** (Pl. 78, Fig. 175). In the molecular layer there are very many **tangential fibers** running parallel to the surface, but not easily demonstrable for the most part, which cross internally in all directions. It is practically certain that we have here, aside from the just mentioned neurites of Martinotti's cells, centripetal fibers that enter from the medulla and end in the cortex. Within the other regions of the cortex we find a fairly uniform **felt of medullated nerve fibers,** in which parallel lines of fibers placed vertically to the surface are met with in the region of the medium sized pyramids, that become stronger as they go deeper, and radiate into the fibrous mass of the medulla. These so-called **radiating bundles** are nothing else than the neurites of the cortical cells, particularly of the pyramidal, united into bundles. Two very striking striæ run parallel to the surface. In one of them are many tangential medullated fibers, while in the other the fibrous plexus shows a material thickening. These are the two **Baillarger's stripes.** The ***outer*** of the two lies in the region of the large pyramidal cells, the ***inner*** one, more weakly developed, as a rule, in the region of the giant pyramidal cells. The tangential fibers running in these stripes are chiefly collaterals of the neurites of the pyramidal cells, but there end here, just as in the molecular layer, many centripetal fibers ascending out of the medulla.

The **neuroglia** of the gray matter of the brain is best developed on the surface, where there is a layer of glia cells that send their processes deeply into the tissue, and we find additional glia cells scattered through the entire cortex. The glia fibers form a dense felt over the cortex that varies in thickness, from which fibers radiate vertically into the tissue. These become fewer the deeper they go, although they again become very numerous in the medulla.

The **arteries** of the cortex form a wide meshed plexus in the pia, from

which branches pass vertically into the tissue. As these do not anastomose they are called ***terminal arteries.*** They penetrate down to the medullary substance, where they break up into capillaries, having given off on the way many lateral branches that supply capillaries to the cortex, forming a plexus that is closest about the pyramidal cells. In addition to these long arteries that pass through to the medulla there are also short ones that break up into capillaries in the gray cortex. The very thin walled and valveless **veins** of the brain follow practically the same intracortical course as the arteries. They start in the medulla and as they pass through the cortex they collect from it its venous blood.

h. The Olfactory Bulb

The **olfactory bulb** receives the **fibers of the olfactory nerve** that pass through the apertures in the cribriform plate of the ethmoid. This bulb is developed to a much greater extent in animals gifted with a sharp sense of smell than it is in man, and its layers are sharply differentiated in them. In such animals it has a cavity, the ventriculus bulbi olfactorii, which is connected with the lateral ventricle of the brain, but in man this ventricle is obliterated and replaced by a mass of glia. It is surrounded by the **medullary substance,** medullary nerve fibers that continue backward in the tractus olfactorius. Ventrally from the medulla lies the **granular layer,** consisting of bundles of medullated nerve fibers much interwoven together, with little nerve cells lying between them. Each of the latter has a neurite that penetrates into the medulla, and several dendrites, one of which always enters the succeeding layer and branches between its cells. This **gelatinous layer,** which adjoins the granular ventrally, is characterized by large nerve cells that are pyramidal in shape, the **mitral cells,** the bases of which are directed ventrally, the apices dorsally. From the apex comes the neurite, which, after giving off several collaterals, turns toward the brain into the medulla. The strong dendrites arising from the base run ventrally and enter the **glomeruli** that are about to be described, where they split up into many fine fibrils. This layer contains smaller nerve cells of Gogli's second type. Next is the **glomerulus layer,** formed of the macroscopically visible **glomeruli olfactorii.** These are spherical corpuscles, measuring about 2 mm, that consist of a very dense felt of very minute nonmedullated nerve fibrils. This felt is formed from the dendrites of the mitral cells, as has been said, with the addition that every fiber from the following, most ventral layer enters a glomerulus and breaks up into very minute fibrils that come into intimate contact with the preceding. This most ventral layer lies directly on the cribriform plate of the ethmoid, and its **fibers** are those of the **olfactory nerve,** which thus end in the glomeruli olfactorii.

4. THE MEMBRANES OF THE CENTRAL NERVOUS SYSTEM

The spinal cord and brain are encapsuled by three connective tissue membranes, the ***dura mater,*** the ***arachnoid,*** and the ***pia mater.***

The **dura,** the outermost of these, has an **outer** and an **inner** layer. The former is attached to the bone by numerous connective tissue fibers and thus forms the internal periosteum of the skull and of the vertebral canal, while the inner adjoins the arachnoid. Both layers consist of connective tissue fibers united into thick bundles that lie close together, and take a uniform course in each, though the direction differs in the two. Between the bundles of connective tissue are elastic fibers that come together to form an outer elastic limiting membrane in the outer layer, and an inner elastic limiting membrane in the inner. The two layers are connected by a thin lamina of loose connective tissue. At the place where the venous sinus is formed the two layers separate and enclose the sinus between them. Several layers of fibroblasts, which correspond to the cells of the fibroelastica of the periosteum, lie outside of the external layer, while toward the arachnoid the connective tissue of the dura is covered by an **epithelium,** a layer of flat cells, the margins of which may be brought out easily by the silver stain.

The dura is connected with the **arachnoid** by sparse trabeculæ of connective tissue, and forms with it a sheath about all the nerves that leave the central organ. They are so closely approximated in most places that the **subdural space** between them is simply a capillary cleft, but as the outer surface of the arachnoid also is covered with **epithelium** this space has an epithelial lining everywhere and is a cavity filled with **cerebrospinal fluid.** It is in open connection with the lymph spaces of the olfactory mucous membrane, the internal ear, and the eyeball, as it extends with the dura upon the **olfactory, auditory,** and **optic nerves.**

The arachnoid is considerably thinner than the dura and has a much looser structure. Its bundles of connective tissue form a loose network which is somewhat thickened both externally and internally. All of the connective tissue bundles of the arachnoid are surrounded by fibers that weave about them and are covered by epithelial cells. It is connected with the pia by similar, very numerous bundles of connective tissue that often are very long, so that an extensive cavity lined with epithelium, the **subarachnoidal space,** exists between the two membranes. This space communicates through the foramen of Magendie and the aperturæ laterales ventriculi with the system of cavities in the brain and spinal cord, and like them is filled with **cerebrospinal fluid.**

In many places the arachnoid sends villuslike processes into the venous lacunæ of the dura, that will be described later. These are the **arachnoidal villi,** or **Pacchionian bodies,** which have the same structure as the arachnoid.

While the dura and the arachnoid pass smoothly over all of the sulci of the brain and spinal cord, the **pia mater** enters each depression and covers uniformly all of the irregularities of the surface. It also sends processes into the brain with the blood vessels to form lymph sheaths about the latter. The

pia consists of a loose connective tissue, is denser and stronger on the spinal cord than on the brain, and contains very many connective tissue cells, which frequently have pigment granules in their bodies.

The **telæ choroideæ** and **plexus choroidei** are villuslike diverticula of the pia into cavities of the brain. Some arachnoidal tissue also always enters into them. In the interior of each arachnoidal villus is a little vascular tree. Toward the ventricle they are covered by the brain wall, which is reduced here to a simple cuboidal epithelium separated from the connective tissue by a membrana propria. Filamentous mitochondria have very recently been demonstrated in the cells, which break down into minute drops of secretion that are extruded from the cells. Lipoid and pigment granules also are met with in the latter.

The **secretion** produced by the cells is the **cerebrospinal fluid,** a limpid, very slightly alkaline liquid that contains at most only 1% of solid constituents, among which are albumose, glucose, and urea.

The **blood vessels** of the cerebral membranes are confined to the dura and pia, the arachnoid is not vascular. The **arteries** of the **dura mater** are very abundant, yet send by far the most of the blood they contain to the diploe of the skull. Two capillary plexuses are formed in the dura itself, one in the inner, the other in the outer layer. The **veins** form similar plexuses and either empty their blood into the sinuses, or accompany the arteries. The dura also has in many places, but especially near the sinus longitudinalis superior, cavities lined with epithelium that are interpolated between the meningeal veins and the sinus, and are known as the **venous lacunæ.** They are in open connection with the veins of the brain and of the diploe.

The **pia** abounds in capillary plexuses that originate from vessels coming out of the brain and spinal cord.

The **nerves** of the dura are sensory branches of the trigeminus, together with fibers that enter with the vessels. They form a wide meshed plexus from which twigs extend with free ends. Nerves have not been demonstrated with certainty in the arachnoid, although the pia is fairly well supplied with them. Sympathetic nerves enter it with the vessels, while sensory branches detach themselves from the outgoing nerve roots and unite with them.

5. THE CEREBRAL GANGLIA

The ganglia of the sensory cranial nerves generally resemble in structure the spinal ganglia, yet in many of them bipolar cells are found together with the typical unipolar ones, and they form the great majority in the ganglia of the auditory nerve (Pl. 29, Fig. 75). Above all the cerebral ganglia are rich in the fenestrated forms described in the spinal ganglia, and lobed cell processes are found more often in them. Moreover most of the cerebral ganglia contain larger or smaller numbers of the sympathetic cells about to be described.

6. THE SYMPATHETIC GANGLIA

The coarse structure of the sympathetic ganglia is similar to that of the spinal. Each ganglion is enclosed in a connective tissue **capsule,** in which

fat cells are often present, and contain **sympathetic nerve cells,** which differ in many ways from the nerve cells of the spinal and cerebral ganglia (Pl. 84, Fig. 184), and are split up into larger and smaller complexes by bundles of nerve fibers that pass through the ganglion (Pl. 84, Fig. 183). The most important point in which the sympathetic differs from other nerve cells is that its neurite becomes in many cases, though not in all, a nonmedullated nerve fiber, i.e., one which is invested only with a sheath of Schwann. This is not a characteristic of all sympathetic cells, for there are some that have neurites invested with medullary sheaths.

Each **sympathetic nerve cell** has a **capsule.** The cell body contains one nucleus, rarely two nuclei, which scarcely differ from those of other nerve cells. Nissl's clods are found in them and frequently present an arrangement that is quite characteristic, the coarser clods lying in the periphery of the cell, while those in the interior are fine and dustlike.

Two principal types may be differentiated from their shapes, ***motor*** and ***sensory cells.*** The **motor cells** are of a roundish or irregular form. The dendrites are strong, but pretty short. The neurite leaves the ganglion as a nonmedullated fiber and terminates on a smooth muscle fiber, though it is quite possible that it may pass to another sympathetic cell and that it is the neurite of this last that reaches the muscle fiber.

The **sensory sympathetic nerve cell** is rather more elongated and is characterized by very long dendrites which either branch in the same ganglion or pass as sympathetic fibers into the epithelium of the viscera, to end there as afferent, sensory, sympathetic fibers. The neurite is usually invested with a thin medullary sheath, leaves the ganglion, and forms a terminal basket about a sympathetic cell in another ganglion.

As has been mentioned in another place, many medullated fibers of the anterior roots pass through the rami communicantes into the spinal ganglia, and also into the sympathetic ganglia of the head. These **afferent fibers,** which come from the cells of the lateral horns, or the motor cells of the cranial nerves, form terminal baskets about the motor sympathetic cells. Yet such fibers may also pass through the ganglia without interruption and accompany the sympathetic fibers to their endings. Other afferent fibers are sensory; they are the dendrites of the sympathetic cells and conduct to the latter stimuli that affect the epithelium of the gastrointestinal mucous membrane.

Besides the ganglia of the great gangliated cord, and the partes abdominalis et pelvina sympathici, the ciliary, sphenopalatine, otic and submaxillary ganglia are composed of sympathetic cells. Nerve cells of the sympathetic type are also found in true cerebral ganglia, as in the ganglion jugulare.

7. THE PERIPHERAL NERVES

Every peripheral nerve is invested with a connective tissue sheath, comparable to the perimysium externum of the muscle, which is called the **epineurium** (Pl. 72, Fig. 166). The bundles of connective tissue in it are arranged rather loosely and irregularly, are accompanied by many elastic fibers, and always include large masses of fat cells. The epineurium everywhere

sends broad longitudinal septa into the nerve, which anastomose and divide it into many **secondary nerve bundles.** Each of these is invested externally with a special thin sheath which is easily distinguished from the epineurium and is known as the **perineural sheath.** It likewise consists of connective tissue, the very slender bundles of which take part in the formation of fine plates concentrically surrounding the secondary nerve bundles, together with sparse elastic fibers. Two such plates are always separated by a continuous layer of flat, polygonal, connective tissue cells that lie close together like an epithelium. It happens that through this abundance of cells, or of protoplasm, the perineural sheath is quite plainly distinguished from the epineurium by its stain (Pl. 71, Fig. 165).

The perineural sheath in turn sends longitudinal septa into the secondary nerve bundles and divides each mass of fibers into the **primary nerve bundles.** This connective tissue, situated within the secondary bundles, is called the **endoneurium,** but this name is also applied to the connective tissue that separates the nerve fibers within the primary bundle from one another. The **endoneural sheath** is distinguished from the endoneurium in the same way as the perineural sheath is told from the epineurium.

The structure and dimensions of the **nerve fibers** that compose the primary bundles have already been thoroughly discussed. Those of the cerebrospinal nerves are for the most part medullated and invested with sheaths of Schwann, yet nonmedullated fibers are always present. In the same way the sympathetic nerves contain medullated along with their nonmedullated fibers.

In its advance toward the periphery the nerve breaks up into separate secondary bundles, which later divide again, so that each minute nerve twig is always provided with a perineural sheath which invests it completely. As soon as the bundle has separated into its individual fibers each of the latter becomes invested by an endoneural sheath, in addition to its sheath of Schwann, which it loses with its medullary sheath. In the case of sensory fibers that enter encapsulated corpuscles this sheath blends with the capsule. In like manner it continues into the spinal ganglia and passes over into the capsule of the cell.

The **blood vessels** of the nerves, which come from the arteriæ comites, form a large plexus in the epineurium from which twigs perforate the perineural sheath and break up in the endoneurium into a longitudinal system of capillary plexuses.

Lymphatics are wanting in the nerves. The lymph circulates in them within the clefts formed by the connective tissue of the endoneurium in the secondary bundles, which are closed externally by the perineural sheath.

Special nerves, the **nervi nervorum,** have been demonstrated within the epineurium, where they end in free arborizations.

IX. THE ORGANS OF SENSE

1. THE EYE

The eye is a very complicated structure, to the formation of which the nerve plate, the ectoderm and the mesenchyma contribute alike. The **perceptive apparatus** comes from the **nerve plate,** the **dioptric apparatus** from the **ectoderm,** the **protective capsule** and the **extrinsic muscles of the eye** from the **mesenchyma.** The first traces of the rudimentary eye appear very early in the embryo in the form of a paired **optic depression** on each side in the anterior part of the brain plate. When the latter forms the cephalic portion of the medullary tube the depression appears like a vesicular diverticulum from its lateral surface, from which develops the **optic vesicle,** connected with the cerebral ventricle by a short canal, the **optic pedicle.** Looked at from the side the vesicle appears flat, rather than like a pouch. It now undergoes an uneven development, as its margins grow faster than its center, so that in time a **cup,** or the **secondary optic vesicle,** is formed, the **distal layer** of which thickens greatly into the cavity, and thus gradually approximates the thin **proximal layer.** Growth is inhibited entirely in the middle of the ventral wall of the cup, so that the latter presents a ventral **ocular cleft,** which continues as a groove on the optic pedicle. In this groove lies the central artery of the retina, which continues through the ocular cleft into the interior of the secondary optic vesicle as the hyaloid artery. The ocular cleft is closed in finally by adhesion of its walls, together with the groove in the distal part of the optic pedicle, and then the central artery of the retina enters the optic pedicle obliquely and comes to lie in the axis of its distal portion with its continuation, the hyaloid artery, passing through the axis of the secondary optic vesicle.

Simultaneously with these changes the rudiment of the **dioptric apparatus** appears. A zone of thickened epithelium, the **lens plate,** may be seen very early in the epidermis lying opposite the distal wall of the optic vesicle; it dips into the **lenticular fossa,** and this deepens to form the **lenticular saccule.** When separated this becomes the **lenticular vesicle,** which is situated just beneath the epidermis with its proximal wall at first closely adjoining the distal, thickened wall of the secondary optic vesicle, but gradually these two separate, leaving between them the **cavity of the vitreous.** The hyaloid artery passes through this to the proximal wall of the lenticular vesicle. All parts of the eye develop from this primitive optic vesicle with its pedicle, the lenticular sac, and the adjacent parts of the mesenchyma and epidermis, as will be shown in detail.

a. The Retina

The **retina** is the most primitive and oldest part of the entire eye. It originates from the epithelial wall of the primitive optic vesicle and is there-

fore really a part of the brain. This wall consists, as we have seen, of two layers that blend at the margin of the vesicle. The **proximal layer** remains thin and is a single layer of cuboidal cells in which **pigment** appears very early. The formation of pigment begins at the margin of the cup and gradually extends proximally until all of the cells are filled with it, and now constitute the **pigment epithelium** of the retina. The proximal always closely adjoins the **distal layer,** which is very thick by contrast, and soon becomes a membrane having many layers. It is only at the margin of the vesicle that the distal layer remains thin, so that the thin margin of the cup, the **pars cæca retinæ,** is always sharply defined from the rest of the retina, the **pars optica retinæ.** The place of transition, an irregular, circular line, is known as the **ora serrata.**

The differentiation of the elements that compose the **pars optica** begins quite early, is ended before birth, and follows in general the same laws as in the spinal cord and brain. A division takes place into supporting and nerve cells, **spongioblasts** and **neuroblasts.** The former permeate the entire thickness of the organ, the same as the ependymal cells, but unlike the latter maintain their form. Only a part of them, confined entirely to the distal part of the retina, change into astrocytes. The majority of the nerve cells are bipolar, the minority multipolar and unipolar. They are arranged in several layers in such a way that every two layers of cells are separated by a layer of fibers in which the processes of the cells come in contact. The most distal layer, bordering on the vitreous, changes to large, multipolar cells, the neurites of which form a continuous layer of nerve fibers on the distal surface. They grow into the epithelial optic pedicle, pass in it to the brain, and thus transform it into the optic nerve. The cells of the most proximal layer develop the power of perception of light and form the layer of rods and cones. From the proximal end of each a process extends toward the pigment epithelium about the third month of pregnancy.

Temporarily from the place of entrance of the optic nerve, in the optic axis, the retina thickens into a **central area** in embryos of the sixth month. This remains for life in most mammals, but in man its center gradually sinks in, as the result of a separation of its distal layers, in the last months of pregnancy, creating a pitlike depression in the retina in the optic axis, the **fovea centralis,** the floor of which is formed by the elements of the most proximal retinal layer alone. The vicinity of this depression, the area centralis, has also been named the **macula lutea,** because it appears yellow in the eye of the cadaver.

A very distinct striation may be seen in the cross section of the retina of an adult, caused by an alteration of layers that are rich and poor in cells (Pl. 86, Fig. 187; Pl. 87, Fig. 188). These layers are from without inward:

1. **The pigment epithelium,** the proximal, thin layer of the optic vesicle that has been described already. This consists of a single layer of cuboidal cells, the surfaces of which present a very regular pentagonal or hexagonal form (Pl. 7, Fig. 22). The cells are three or four times as broad as high and are joined together by a cement. Each sends from its inner, distal surface numerous threadlike processes between the elements of the follow-

ing layer. These, as well as the distal part of the cell body, contain granules, needles, and rods of a pigment, **fuscin,** which contains iron, is insoluble in water, alcohol and ether, and can be bleached by nascent chlorine (Pl. 7, Figs. 23 and 24). It is caused to move by the influence of light. In the dark the pigment draws back into the cell body, but in the light it streams into the processes.

2. **The layer of rods and cones** is also called the **neuroepithelium,** and contains the **percipient elements,** the ***rods*** and ***cones,*** which are, as we have seen, processes from the most proximal layer of cells of the distal lamina of the retina (Pl. 87, Fig. 188). The **rods** are cylinders about 60 μ long by 2 to 3 μ broad, which may be divided into ***outer segments,*** 35 μ long, and rather shorter ***inner segments.*** The **outer segment** is uniformly thick throughout its entire length, is strongly refractive to light, and readily breaks down in consequence of post mortem maceration into numerous successive platelets. It has a firm capsule with myelinlike contents. The former contains a spiral thread and fine longitudinal fibrils. The outer segment is always sharply defined from the inner and is saturated during life with an easily destroyed red coloring matter, the **visual purple,** or **rhodopsin,** that is quickly bleached by the action of light and is regenerated in the dark under the influence of the pigment epithelium. The **inner segment** is always shorter than the outer and is not uniformly thick, but is somewhat swollen in the middle. It is less refractive than the outer segment, the capsule and fibrils of which are continuous over it. It contains in its distal portion many short, rigid threads that stain more strongly with most dyes than any of the other parts of the rod and form what is known as the **rod ellipsoid.**

The **cones** are shorter than the rods and are likewise divided into ***inner*** and ***outer segments.*** The outer segment is short and conical, the inner is longer, barrel-shaped, and twice as thick as the inner segment of the rod. Otherwise all of the structural peculiarities of the rods are repeated in the cones. The distal part of the cone is contractile and shortens under the influence of strong light; it is therefore known as the **cone myoid.** The **cone ellipsoid,** situated proximally to it, is always very distinct and well developed.

3. **The limitans externa.** The inner segments of the rods and cones are bounded distally by the delicate, but sharply defined, membrana limitans externa, which is perforated like a sieve to permit the passage of the continuations of the rods and cones through its apertures into the next layer. The peculiarities of its structure, as well as its importance, will be dealt with in the description of the supporting cells.

4. **The outer granular layer** is the most conspicuous of all of the layers of the retina and exhibits, when stained in the usual manner, six or more rows of densely packed nuclei. If specific methods of staining are employed, these nuclei may be seen to belong to two different kinds of cells (Pl. 88, Fig. 189). As indicated above, the inner segment of each cone passes through the limitans externa, continues into the outer granular layer, and passes over into a cell body lying just beneath this membrane, the **cone granule,** its secretory product. All the cone granules lie in a single row just beneath the limitans externa. The cone granule and the inner segment

of the cone are of about the same thickness and differ but little from each other. Distally the cone granule suddenly tapers off into a **cone fiber,** which passes in a straight or somewhat curved course through the outer granular layer and the succeeding Henle's layer of fibers, to end in an expansion, the **cone foot,** in the outer plexiform layer, from which little terminal twigs radiate. The entire formation, the cone with its outer and inner segments, the cone granule, cone fiber, and cone foot, we know as the **cone optic cell.** The relations of the **rod optic cell** are somewhat different. The inner segment of the rod continues in a slender fiber on this side of the limitans externa, swells out within the outer granular layer into a little cell body with a nucleus, the **rod granule,** to immediately become filiform again and to extend as a **rod fiber** to a little **terminal nodule** in the outer plexiform layer. The rod granules are rather smaller than the cone granules and lie close together at all levels in the outer granular layer.

5. **Henle's fibrous layer** is formed by the strong **cone fibers,** and consequently exhibits a striation vertical to the surface of the retina. It is very narrow, as is also the following.

6. **The outer plexiform layer** contains the footlike ends of the cone fibers and the knoblike ends of the rod fibers, together with the terminal arborizations of the bipolars soon to be described.

7. **The inner granular layer** emulates in extent the outer granular layer, and like it shows several layers of nuclei by the ordinary methods of staining, which are not usually packed so closely together. They belong to various kinds of cells, the most important of which are known as the ***rod*** and ***cone bipolars*** (Pl. 88, Fig. 189). The **rod bipolar** has a spherical or pyriform cell body, and passes proximately into a short, necklike process, which very soon splits into numerous fibrils in the outer plexiform layer. They always have quite a number of end nodules of the rod optic cells between them. Distally the cell body changes into a long fiber that passes through the inner granular layer and the succeeding inner plexiform layer, breaks up into several short processes, and embraces with them the body of a large ganglion cell. The **cone bipolar** has a similar structure. Its cell body is rather smaller, its proximal process rather longer. It breaks up in the outer plexiform layer into a flat, spreading terminal arborization, and comes in contact here with the cone foot piece. The distal slender process penetrates for a greater or less distance into the inner plexiform layer, and terminates with several short, strong end twigs.

The second kind of cells of the inner granular layer is the amacrine. The **amacrine cell** has a body that is usually rather longer than that of the bipolar, and a single process which runs distally to various levels in the inner plexiform layer and breaks up into terminal twigs that run horizontally. Thus there are found in this layer as many as six sublayers of amacrine terminal fascicles. Other amacrine cells send their terminal twigs through the entire inner plexiform layer, and are known as **diffuse amacrines** to distinguish them from the others which are called **stratifying.**

A third variety is the **horizontal cells,** which lie in the proximal districts of the inner granular layer and may also extend into the outer plexiform

layer (Pl. 88, Fig. 189). Short processes from the elongated cell bodies radiate into the latter and unite here with the knoblike ends of the rod optic cells. A longer process extends from one end of the cell body horizontally through a larger extent of the outer plexiform layer, to finally likewise break up into a terminal fascicle, which in turn surrounds a group of the button-shaped ends of the rods.

Mueller's cells form the last variety to which the nuclei of the inner granular layer belong. These will be described later.

8. **The inner plexiform layer** is also very extensive. It contains the distal branchings of the cells of the inner granular layer, which unite here with the expansions of the proximal processes of the ganglion cells.

9. **The layer of ganglion cells** is formed of typical, large nerve cells with distinct Nissl's clods and neurofibrils (Pl. 87, Fig. 188). The cell body sends out one or more dendrites into the inner plexiform layer, which either pass through or spread out in it horizontally at various levels, so that their branches form laminæ that correspond to the expansion of the amacrines and the distal terminal arborizations of the cone bipolars. The neurite usually goes off at a right angle from the distal surface of the cell and enters the layer of nerve fibers as a **nerve fiber.** The distal terminal twigs of the rod bipolars closely adjoin their cell bodies (Pl. 88, Figs. 189 and 190).

10. **The layer of nerve fibers** consists of **nonmedullated nerve fibers** that assemble into bundles and take their way to the papilla in order to pass through it into the optic nerve. The great majority of these fibers are the neurites of the ganglion cells that have just been described, and hence conduct **centripetally,** but associated with them are **centrifugal** fibers that come through the optic nerve from the cells of the brain, pass through the layer of nerve fibers to the inner plexiform layer, and there break up into terminal arborizations which come into close relations with the amacrine cells.

11. **The limitans interna** is the innermost layer of the retina, and is, like the limitans externa, composed of supporting elements.

These **supporting elements** of the retina appear in two different forms, as ***Mueller's,*** or ***radiating, fibers*** and as ***astrocytes.*** **Mueller's fibers** are best compared with the embryonal ependymal cells of the medullary tube. Like them they are long, cylindrical and rodlike formations that pass through the retina from the limitans externa to the limitans interna in a course that is perpendicular to the surface. At both ends they spread out in footlike expansions that are cemented firmly together so as to form the two limiting membranes, the **limitans externa and interna,** which are therefore not independent layers or membranes, but are the connected expansions of these fibers (Pl. 87, Fig. 188). Processes extend from the entire length of each of Mueller's fibers, some filamentous, some membranous or winglike, which penetrate between the nervous elements of the different layers of the retina, sheathe them, and anastomose with the processes of neighboring Mueller's fibers. A supporting fibrous framework is thus produced that pervades the entire retina. Fine fibrils run through the entire length of the cell body and spread out like brushes in the expansions. These fibrils resemble fibers of

neuroglia in their staining reactions. From the proximal end of each of Mueller's fibers, therefore from the limitans externa, minute fibrils radiate out and form fibrillary baskets about the inner segments of the rods and cones. The fibrils lie within the homogeneous protoplasm of the cell body, which frequently appears indented by the neighboring nerve cells. The nucleus of a Mueller's fiber is found within the inner granular layer and commonly stands out laterally from the periphery of the cell.

The **astrocytes** of the retina are exactly like those of the central nervous system. They are found chiefly in the layer of nerve fibers and penetrate with these into the optic nerve. They are met with much more rarely in the proximal layers.

Having thus learned the constituent elements of the retina, we have to study their relations in the different parts, beginning at the papilla and proceeding distally to the ora serrata. The **papilla of the optic nerve** itself contains no nervous elements except the optic fibers, and is therefore known as the **blind spot** (Pl. 86, Fig. 187). The retina here is cut out, as it were by a punch. All of the fibers in the layer of nerve fibers converge to this hole, pass through it and form the optic nerve. Hence the papilla has a funnel-shaped depression in its center, the **excavatio papillæ nervi optici,** from the bottom of which the central vessels rise into the retina.

All of the layers of the retina are best developed in the ***vicinity of the papilla.*** The layer of nerve fibers is naturally particularly thick, because it is here that its elements are most accumulated. The cells of stratum gangliosum form several layers. The rods and cones alternate in the neuroepithelial layer, every two cones being separated by one or two rods.

If we proceed distally toward the temporal side we approach the **macula lutea,** which may be recognized by the fact that the ganglion cells are heaped up still more and form as many as eight layers in the stratum gangliosum. The rods become fewer in the neuroepithelium, while the cones become longer and assume more nearly the shape of rods. Henle's fibrous layer becomes very marked and distinct, thanks to the cone fibers. The entire thickness of the retina at this place is about 5 mm.

The **fovea centralis** is an oval depression in the retina, measuring 0.2 by 0.15 mm, the margins of which slope gradually (Pl. 86, Fig. 187). Its floor is formed wholly of pigment epithelium and very long **cone cells.** Rod cells are entirely absent. The cone granules lie in two or three layers and extend somewhat back of the limitans externa. The cone fibers arch laterally from the bottom of the fovea to the cone bipolars in its margin, which are arranged obliquely to the surface of the retina. In the wall of the fovea the ganglion cells form first a single layer, then more, up to as many as eight layers. Mueller's fibers run obliquely to the surface of the retina in the margin of the fovea.

The farther we go **distally** from the fovea centralis the **thinner** the retina becomes. This thinning affects first and chiefly the layers of nerve fibers and of ganglion cells. In the latter the cells very soon form only a single layer which presents breaches of continuity that become more frequent the farther we go. The cones, which alone were present in the fovea centralis, gradually

become displaced by the rods, though both are always present. Each cone is separated from its neighbor at first by one, later by from two to five rods, so that the number of rods in the entire retina is twenty-three or twenty-four times that of the cones. The gradual disappearance of Henle's fibrous layer corresponds to the decrease in the number of the cones.

The retina in the **distal portion** of the pars optica has a thickness of only 0.15 mm; it then suddenly passes into the pars cæca, which is only 0.05 mm thick (Pl. 85, Fig. 185). This region of transition is called the **ora serrata.** The ganglion cells disappear first, and naturally with them the layer of nerve fibers. The outer plexiform layer tapers off quickly, while with its disappearance the inner and outer granular layers blend and contain many vacuoles that are often of considerable size. The nuclei in the blended granular layers belong for the most part to Mueller's fibers, which are very dense at this place. We find no rods and only stunted cones in the neuroepithelium. Finally, there remains in the pars cæca only a double layer of cells, the outer of which is formed of cuboidal pigment epithelial cells that are now without processes, while the inner consists of a single layer of cylindrical cells. This epithelium continues over the ciliary body and is then known as the **pars ciliaris retinæ.**

b. The Optic Nerve

As we have seen in the review of the embryology, the optic nerve comes from the **optic pedicle,** which is very short at first, but later elongates a great deal. Its lumen communicates with the ventricles of the brain, and its wall consists of several layers of cylindrical cells. Inasmuch as the optic cleft continues for a distance on the optic pedicle, its ventral surface presents at first a groove in which the central artery and vein come to lie. The lumen is displaced dorsally, is much contracted, and finally is completely occluded, after the closure of the groove, by a lively proliferation of the epithelium, so that the **optic pedicle** is then a **massive cellular formation.** Before the disappearance of the cavity **nerve fibers** from the young retina grow out into the pedicle and use it as a **path** to conduct them to the brain. The farther these fibers progress the more they force apart the epithelial cells of the pedicle, which become **glial elements** between them. Later connective tissue also takes part in the structure of the nerve, part of it coming from outside, part from the central vessels, and divides the fibers into separate bundles.

The three cerebral membranes combine to form a **connective tissue investment** for the optic nerve at its exit from the skull, that covers it throughout its intraorbital course. The dura mater remains distinct and forms the **outer sheath,** while the arachnoid and pia mater blend to form the **inner.** Between the two lies a continuation of the **subdural space** lined with epithelium, while within the inner sheath is a system of clefts that communicates with the **subarachnoidal space** of the brain. The two sheaths blend at the eyeball and pass over into the sclera (Pl. 86, Fig. 187).

The inner sheath lies close to the nerve and sends into its substance many anastomosing septa which unite with the connective tissue entering the nerve with the central vessels in the distal segment. These vessels, the **central artery**

and vein of the retina, penetrate obliquely into the trunk of the optic nerve 7 or 8 mm distant from the eyeball, and then form with the connective tissue about them the **axis** of the nerve.

The connective tissue septa divide the optic nerve into between eight and twelve hundred **bundles** of unequal size, but do not invade the interior of these bundles, each of which consists of **medullated optic nerve fibers** of varying sizes that **have no sheaths of Schwann,** the same as all central nerve fibers. Many **astrocytes** are to be found within the bundles, with their glia fibers running for the most part vertical to the course of the nerve fibers. These astrocytes are, as we have seen, the remains of the former epithelial cells of the optic pedicle.

On arriving at the eyeball all of the fibers of the optic nerve lose their medullary sheaths, and the nerve trunk consequently becomes considerably more slender. At the same time it passes through the so-called **lamina cribrosa** in a very large number of little bundles of **nonmedullated fibers.** The lamina cribrosa is a cribriform plate of connective tissue that closes the aperture in the eyeball for the entrance of the optic nerve, and is situated at the place where the sheaths of the optic nerve pass into the sclera. It is reinforced by many blood vessels which unite the central artery and vein of the retina, before they enter the excavation of the papilla, with the short posterior ciliary arteries and veins.

Having arrived at the **papilla** the fibers radiate in many little bundles in the layer of nerve fibers of the retina. One bundle, the **papillomacular,** goes directly to the macula lutea, the rest radiate in all directions and frequently interlace. We must remember that these bundles are composed of *naked axis cylinders with neither medullary nor Schwann's sheaths.*

c. The Choroid

The epithelial optic vesicle is surrounded very early by numerous blood vessels embedded in the mesenchyma. Toward the end of the third or the beginning of the fourth embryonal month these vessels present a typical arrangement, in that the larger ones lie farther out, while the capillaries lie close to the pigment epithelium. Pigment granules soon appear in the connective tissue cells lying between the vessels, the entire vascular membrane becomes sharply defined from the nonvascular connective tissue outside of it, and may then be known as the choroid.

The **choroid** directly adjoins the outer surface of the retina and contains the **blood vessels** that supply the proximal layers of the latter with nutriment. It ends with a fairly sharp margin at the entrance of the optic nerve, and passes over into the biliary body at the ora serrata, and presents the following layers from within outward:

The **lamina basalis** directly adjoins the pigment epithelium, with which it is more or less firmly connected, and consists of two layers, the inner of which is structureless, while the outer is a very finely fibrillar network of elastic fibers known as the stratum supracapillare. Both together are only about 2 μ thick in young eyes, but may be considerably thicker in old age.

The **lamina choriocapillaris** contains exclusively ***capillary vessels***

embedded in a homogeneous, structureless basal substance bounded externally by a finely fibrous elastic limiting membrane (Pl. 87, Fig. 188).

The **lamina vasculosa** embraces the ***arteries and veins*** belonging to these capillary vessels, so the coarser vessels lie to the outer side of the finer. Membranes formed of bundles of connective tissue lie between the vessels. They are abundantly provided with elastic networks, and also contain many connective tissue cells with bodies permeated with black or brown **pigment granules.**

The **lamina suprachoroidea** joins the choroid to the sclera, to which it may be said to belong. It consists of several lamellæ of connective tissue, strongly reinforced by elastic fibers that anastomose. Pigmented connective tissue cells lie in the lamellæ, and upon them are connective tissue cells containing no pigment and arranged as in an epithelium. Between the lamellæ are the **perichoroidal spaces,** which are filled with lymph.

d. The Ciliary Body

The primitive condition of the margin of the optic vesicle is maintained comparatively long. Even at the beginning of the third fetal month it appears as a narrow, thin continuation of the retina, the **pars cæca retinæ.** Outside of it lies the connective tissue and vessels of the choroid, which more distally is continuous with the pupillary membrane to be described later. In the middle of the third month a marked longitudinal growth takes place in the pars cæca retinæ which, together with the great general enlargement of the eyeball, simulates a recession of it proximally. The distally developing part of the pars cæca is the rudiment of the **iris,** the **ciliary body** develops from the rest, together with the externally adjoining mesenchyma. The vascular mesenchyma proliferates toward the interior of the eyeball in the form of meridionally running **folds** in which each vessel comes to be covered on the inner side by the pigmented **pars cæca retinæ,** which now assumes the characteristics of an **epithelium** over these folds. Thus, toward the end of the third month, the rudiment of the **ciliary processes** appears, rising slowly at first from the connective tissue of the ciliary body and then rapidly sloping away distally. In the fourth month **muscular elements** appear in the connective tissue of the young ciliary body, formed by the development of smooth muscle fibrils in the mesenchymatous cells. These have at first a purely meridional course, but circular fibers are added later. The ciliary body is enlarged by the development of the **ciliary muscle,** so that in cross section it protrudes as a triangular mass into the interior of the globe. The ciliary processes rise from its inner surface, slowly decline proximally into the orbicularis ciliaris and slope distally to the root of the iris.

The **ciliary body** of the adult is the direct distal continuation of the choroid, in which the typical arrangement of the vessels is completely effaced by the interpolated ciliary muscle that predominates over the entire structural picture (Pl. 85, Fig. 185). There remains of the choroid externally the **lamina suprachoroidea,** which bounds the ciliary body toward the sclera, and the **lamina basalis** internally, which is continuous over the orbicularis ciliaris and the ciliary processes next the **epithelium.** The latter lies upon a

finely fibrous connective tissue carrying the blood vessels, which forms the framework of the ciliary processes, surrounds the ciliary body, and is known as its **ground plate.** The entire interior of the ciliary body between the suprachoroidea and the ground plate is filled by the **ciliary muscle.** Its bundles of muscular fibers are divided by vascular connective tissue, which is a direct continuation of the connective tissue of the lamina vasculosa and like it carries vessels.

The **ciliary muscle** consists of bundles of ***smooth muscle fibers*** that may be seen to take three courses. The most external ones, adjoining the suprachoroidea, arise from the connective tissue of the lamina vasculosa choroideæ, take a purely **meridional course** distally and are inserted into the region of the scleral protuberance to be described later. This is called the **tensor choroideæ.** Farther inward are bundles that arise from the region of the root of the iris, radiate apart proximally and inwards and are inserted into the ground plate; these are the **radiating bundles.** Quite internally are bundles that have a **circular** course and, unlike the two just mentioned, are cut across in a meridional section; these are the **circular bundles,** or **Mueller's muscle,** and form as a whole the distal part of the muscular ring that surrounds the contents of the eyeball. Between the muscular bundles lies fibrillary connective tissue with numerous elastic fibers, in which we meet with large blood vessels and capillaries, as well as extremely numerous nerve fibers and cells.

The ciliary muscle is very important physiologically as it produces the condition known as **accommodation,** which will be discussed under the subject of the lens and the zonula ciliaris.

The connective tissue is continuous internally with the **ground plate** from which the ciliary processes arise. It continues proximally in the tissue of the **orbiculus ciliaris,** which is essentially the lamina vasculosa choroideæ, but lies directly on the lamina basalis as the lamina choriocapillaris is wanting. The inner surface of the orbiculus ciliaris lies in many low, meridional folds that blend distally to form seventy or eighty **ciliary processes.** These rise gradually for a distance of 2 or 3 mm, have secondary, foldlike elevations on their tops, and suddenly slope away to the root of the iris. Each process consists of the connective tissue of the ground plate, contains many vessels, and is separated from the epithelium by the lamina basalis.

The **epithelium,** the **pars ciliaris retinæ,** is a direct continuation of the retina in the region of the ora serrata. It covers the entire surface of the orbiculus, ciliary body, and ciliary processes, and blends at the root of the iris with the epithelium of the posterior surface of the latter, forming the pars iridica retinæ. It presents a **double layer,** the outer of which, the continuation of the **pigment epithelium** of the retina, is composed of high cuboidal cells so densely filled with pigment granules that it is difficult to perceive their margins. The inner layer, on the contrary, is free from pigment, is the continuation of the **distal layer of the retina,** and consists of cylindrical cells that decrease somewhat in height distally from the orbiculus. Fine fibrils appear everywhere within these **unpigmented cells,** especially in the areas of epithelium that cover the depressions between the ciliary processes, continue into the interior of the globe, and approach the equator of the lens as the zonula

ciliaris. Mitochondria have been found in these cells that produce a secretion which has been demonstrated in the form of minute drops in the cell body. The **secretion of the aqueous** therefore has been ascribed to the inner layer of the pars ciliaris retinæ.

e. The Iris

As shown in the preceding section the iris originates through the growth forward of the two layers of the pars cæca retinæ toward the lens in about the third fetal month. Its lateral surface is covered with mesenchyma that extends in a thin layer over the distal surface of the lens and forms the **pupillary membrane.** At the margin of the optic vesicle the nonpigmented distal retinal layer passes over into the pigmented proximal layer, yet in such a way that the marginal zone has little or no pigment. In the fourth month **smooth muscle fibrils** appear in the distal cells of the proximal layer in the immediate vicinity of the margin, the young muscle cells separate more and more from the epithelium, come to lie in the mesenchymatous tissue as the **sphincter iridis,** and the fibers gradually assemble into several circular bundles. Thus we have a muscle that originates from the epithelium of the optic vesicle, and therefore from the **ectoderm.** Toward the end of the fifth month muscular fibrils appear throughout the entire region of the proximal pigmented epithelium of the now much elongated rudimentary iris, at first lying scattered about in the cells, later assembled on the distal side of the epithelium bordering the connective tissue, and form a coherent layer that extends from the root of the iris to the margin of the pupil and is known as the **dilatator iridis.** Thus we see that the epithelium and the muscles of the iris originate from the ectoderm. The distal epithelial layer has no pigment until the sixth month, when the formation of pigment begins in its cells and advances from the margin of the pupil to the root of the iris.

To this **ectodermal** portion is added a **mesenchymal,** which lies to the distal side of the former and is identical with the **pupillary membrane.** This consists of connective tissue that proliferates with blood vessels toward the lens and forms a fairly thick layer even in the fifth month. At first it passes directly from the margin of the pupil into the pupillary membrane, but the relations are changed later as the pupillary margin of the iris grows forward behind the pupillary membrane, so that the place of attachment of the latter is displaced to the anterior surface of the iris. The pupillary membrane is adherent at its center to the lens capsule, has an extensive vascularization, and undergoes involution after the eighth month through obliteration of these vessels and absorption of its tissue from the center toward the periphery.

The iris consists of three parts which are, from the distal to the proximal (Pl. 85, Fig. 185):

1, The **iris stroma.** This is the mesenchymatous portion and consists of very loose, fibrous connective tissue, the bundles of which interlace and leave intermediate spaces, some larger, some smaller. The connective tissue is very abundantly supplied with branched **stroma cells,** the processes of which anastomose, with the body of each filled with **pigment granules** in accordance with the general degree of pigmentation of the person. When the amount

of pigment is great the color of the iris is black, when less it is brown, and when the stroma contains no pigment the iris is blue. The stroma of the iris is very **vascular,** and the connective tissue is always better developed about the vessels. The connective tissue cells form several layers on its distal surface, known as the **anterior limiting layer.** Toward the anterior chamber the cells form a more or less uninterrupted coat which is called the **anterior epithelium** of the iris.

2. The **sphincter iridis** lies within the stroma in the pupillary portion of the iris. It is a narrow, circular band, about 1 mm broad, that lies nearer the proximal than the distal surface. Its bundles of **smooth muscle fibers** are circular and exhibit manifold anastomoses with the fibers of the following muscle.

3. The **dilatator iridis** is a layer of radiating smooth muscle fibers about 2 μ thick. It lies between the stroma and the posterior epithelium and is also called **Bruch's membrane.** Beyond doubt these muscular fibrils originate from the cells of the parietal layer of the retina, and the only question is whether they remain permanently connected with their mother cells, as indicated by the absence of nuclei, or have a certain independence.

4. The **posterior epithelium of the iris** has a **double layer.** It ends at the margin of the pupil, turning back over it like a hook. All of its cells are so stuffed with **pigment granules** that the cell boundaries cannot be made out. It is only in albinos that this pigment is absent, and its lack then gives the iris a red color. Both layers pass over into the pars ciliaris retinæ at the root of the iris, where the posterior loses its pigment.

The iris has the important duty of **regulating the quantity of light** admitted to the eye; the pupil contracts when the light is strong, and dilates when it is weak. It also excludes marginal rays that interfere with the production of a distinct image.

f. The Lens

We have learned that in a human embryo about 6 mm long the lens is an epithelial vesicle cut off from the ectoderm. It lies just beneath the epidermis, but gradually becomes separated from it by the developing anterior vitreous and the mesenchyma growing in between the two. Very soon after the separation the epithelium of the lenticular sac exhibits an irregular growth. The distal half of its wall remains low while the cells in the proximal elongate more and more until they approach so close to the proximal surface of the distal wall as to obliterate the cavity of the vesicle toward the end of the second fetal month. We call the low cells of the distal wall the **lenticular epithelium,** the elongated ones of the proximal wall the **lenticular fibers.** The two blend at the **equator of the lens.** When the fibers have attained a certain length their capacity for segmentation ceases, they simply grow and leave the production of new fibers to the lenticular epithelium. The cells of the latter divide in the region of the equator, grow into lenticular fibers, while new fibers are formed through constantly renewed cells that are arranged in the form of radiating laminæ. A cleft, that later becomes a three rayed star, appears on the distal and proximal surfaces of the organ where the ends of the fibers meet.

The cells of the lenticular vesicle send out short processes, the so-called **lenticular cone,** from which fine fibrils extend and help to form the primitive vitreous surrounding the lens. But the lenticular cone soon disappears, and in its place the cells of the lenticular vesicle secrete a structureless membrane that envelops the young lens on all sides, and is known as the **lenticular capsule.** This is adjoined externally by vascular connective tissue that forms the **membrana vasculosa lentis,** which is connected distally with the **pupillary membrane,** and is entered at the proximal pole of the lens by the branches of the hyaloid artery. The involution of this begins in the eighth fetal month and proceeds simultaneously with that of the pupillary membrane.

We have to study in the adult lens the capsule, the epithelium, and the fibers (Pl. 85, Fig. 185).

The **lenticular capsule** is a pellucid, structureless membrane composed of separate lamellæ. Its greatest thickness is 15 μ at the distal pole of the lens, from which point it diminishes steadily over the equator to the proximal pole, where it is only 5 μ thick. The part covering the distal surface is commonly called the anterior capsule of the lens, the rest the posterior capsule. It possesses a certain degree of elasticity and is closely related chemically to the membranæ propriæ, which it also resembles in its development. An albuminoid called membranin has been demonstrated in it.

The **lenticular epithelium** is a single layer of cells that covers the proximal surface of the anterior lenticular capsule. These cells are only 2 to 3 μ high in the region of the distal pole of the lens, gradually become higher proximally to pass over into the **lenticular fibers** in the region of the **equator.** They are always placed with their longitudinal axes oblique to the surface of the lens, from which their nuclei are distant, and the distal ends of the constantly lengthening cells overlap their predecessors until the fibers have a course almost parallel to the surface and give rise in the equatorial region to the so-called **vortex,** or **radii lentis.**

The **lenticular fibers** are long, bandlike formations arranged in **radiating lamellæ.** Each lamella consists of a layer of fibers and is connected very firmly with its neighbor (Pl. 85, Fig. 186). ***Mantle fibers, transitional fibers,*** and ***central fibers*** may be distinguished in each lamella. The **mantle fibers** are fairly regularly hexagonal on cross section, three to four times as broad as thick. Each has a **nucleus** in the region of the equator. Toward the interior of the lens the thickness of the fibers increases gradually, the cross section becomes irregular, and the nucleated mantles pass over into the **nonnucleated transitional fibers.** The **nucleus of the lens** is composed of quite irregular, nonnucleated **central fibers.**

The mantle fibers have a soft, semifluid protoplasm that condenses at the surface into a firm crusta. In the transitional fibers, and still more in the central, the protoplasm becomes more fixed and firm, so that the nucleus of the lens is a very resistant, unchangeable mass, while the peripheral layers of fibers readily undergo changes of form, at least until manhood, but in old age they also become fixed.

The lenticular fibers consist chemically of about 63 or 64% water and the

balance of solid constituents, mainly albuminoids, albumoid and crystallin, together with lecithin, cholesterin, fat, and inorganic salts.

Each lenticular fiber is an **S-shaped band,** the two ends of which are situated in different planes. It passes from a point in the distal portion to a point in another plane in the proximal portion, crossing the equator. In both portions of the lens the fibers assemble into radiating surfaces that tend to place themselves vertically to these planes. These commissural surfaces appear in incompletely macerated lenses in the form of two stars, the **lenticular stars,** which are so placed that the radii correspond to the distal, the interradii to the proximal.

The lens, together with the cornea, form the **dioptric apparatus** of the eye, the function of which is to throw a sharply defined, inverted image of any given object into the fovea centralis. During rest the eye is adapted to infinity, the ciliary muscle is completely relaxed and thus exerts a strong traction on the lens through the zonula that connects the ciliary body with the lenticular surface and thereby causes the lens to be flattened. If we wish to see distinctly an object at a finite distance, we contract our ciliary muscles and relax the zonula sufficiently to allow the elasticity of the lens to curve it enough to throw a distinct picture of it into the fovea. The nearer the object is placed, the stronger must be the contraction of the ciliary muscle and the greater the curvature of the lens produced. The less curved anterior surface is affected more than the posterior so that the difference in curvature between them is more nearly equalized. This process is known as **accommodation.** Its amplitude gradually decreases in later life in consequence of the increasing rigidity of the mantle fibers, until the eye is more or less without accommodation in old age.

g. The Cornea

When the lenticular vesicle separates from the ectoderm the latter consists of a single row of cuboidal cells that, so far as it lies in the region of the optic vesicle, provides the anterior epithelium of the cornea. The narrow space between the lenticular vesicle and this epithelium is filled immediately after its origin by fine fibrils that come partly from the proximal surface of these epithelial cells, partly from the cells of the lenticular vesicle, unite and form the **anterior vitreous,** which is continuous proximally with the posterior vitreous. The corneal epithelium soon becomes of two layers, shows a distinct membrana propria, and at the same time cells from the mesenchyma surrounding the margin of the optic vesicle penetrate between the lens and the epithelium, unite with the elements of the anterior vitreous, and gather into several layers on the membrana propria. Proximally the pupillary membrana develops from the margin of the vesicle to the distal surface of the lens, while between it and the layers of mesenchymatous cells the anterior vitreous dissolves and gives place to a cavity called the **anterior chamber.** At this time the cornea consists of two or three layers of **epithelial cells** and several layers of **connective tissue cells.** In the most proximal layer of the latter the cells lie close together so as to form a single layer of epithelium that bounds the rudimentary cornea toward the anterior chamber, the **posterior corneal epithe-**

lium. Proximally the anterior epithelium of the cornea blends with the epithelium of the conjunctiva, the corneal mesenchyma with the rudiment of the sclera. Toward the end of the second fetal month the mesenchymatous cells of the corneal rudiment begin the production of **collagenous,** later of **elastic fibers,** which cause the cornea to increase considerably in thickness. This young **substantia propria** is limited proximally, toward the end of the third month, by a homogeneous membrana propria secreted from the cells of the posterior corneal epithelium, which soon increases in thickness and becomes known as **Descemet's membrane.** Later it condenses distally against the anterior epithelium to form **Bowman's membranes.** The corneal rudiment is nonvascular from the first.

The individual layers of the adult cornea, thus derived, exhibit the following structure:

The **anterior epithelium** has an average thickness of 0.1 mm, is **stratified, flat,** and consists of from five to seven superimposed layers, the deepest of which is composed of low cylindrical, the next two to four of polyhedral, and the final two of flat cells that never cornify (Pl. 10, Fig. 31). In the deeper layers the cells are separated by fine intercellular spaces permeated by plasmodesmi, but those of the superficial flat layers are closely approximated. Mitoses are often met with in the basal cells. Proximally the epithelium passes over into that of the conjunctiva bulbi with a little thickening.

Bowman's membrane, or the **anterior limiting membrane,** is, as we have seen, nothing else than a condensed, nonnucleated part of the substantia propria. Its maximum thickness is 20 μ, and it ends at the periphery of the cornea (Pl. 85, Fig. 185).

The **substantia propria** forms about nine tenths of the entire cornea. It is 0.7 mm thick at its apex and 0.9 mm at the periphery. It consists of somewhat flattened, long **connective tissue fibers** about 10 μ thick, united into about sixty superimposed **laminæ.** Although in general the fibers within the laminæ are parallel to the surface of the cornea, yet there are many that pass from one lamina to another. It is only in the distal layers that we find fibers which take an oblique, or even vertical course, pass through several lamellæ and enter Bowman's membrane, the fibræ arcuatæ. The separate fibers are bound together within the laminæ by a special **cement,** which likewise joins the individual lamellæ. The cornea also contains fine **elastic fibers,** which are most numerous in the proximal layers of the substantia propria. The cellular elements of the basal substance of the cornea are the **corneal corpuscles** (Pl. 89, Fig. 191). These are flat cells with large nuclei, double central bodies, and numerous branching **processes** lying on the connective tissue lamellæ. The processes of the different cells anastomose with those of their neighbors in both the same and neighboring lamellæ, and thus form a **protoplasmic network** through the entire substantia propria, situated within a **system of lymph canals.** This system of canals is not completely filled by the cells and their processes, but contains with them the lymph that serves for the nutrition of the cornea. Wandering cells are commonly met with in them.

Descemet's, or the posterior limiting membrane, is as we have

learned, a secretory product of the cells of the posterior epithelium. It is 6 or 7 μ thick at the apex of the cornea, 10 to 12 μ at the periphery, then it becomes very thin, enters the framework of the sinus of the anterior chamber and disappears. Descemet's membrane is **structureless** and is very closely related chemically to the lenticular capsule, which also is a cellular, secretory product. It is very firmly adherent to the substantia propria.

The **posterior epithelium** of the cornea is a **single layer of flat cells** that are for the most part regularly pentagonal or hexagonal, and about 2 or 3 μ thick. Each cell contains a slight nucleus that presents many forms and is often kidney or bean shaped. Near it lie two central bodies surrounded by a basketlike central capsule, the **centrophormium.** Crystalloids of an albuminoid substance also have been found in it. The distal part of the cell contains epithelial fibers that pass from one cell into another

h. The Sclera

The sclera, the outermost membrane of the eye, is the direct proximal continuation of the cornea (Pl. 85, Fig. 185). The sclerocorneal margin runs obliquely from without inward, so that the distal lamellæ of the cornea end sooner than the proximal. The sclera blends with the sheath of the optic nerve at the entrance of the latter. Here it attains its greatest thickness, 1 to 2 mm, which gradually diminishes distally to 0.3 mm, to increase again to 0.6 mm at the insertions of the extrinsic muscles. The fine trabecular formation of **Tenon's space** is given off from its outer surface. Its inner surface is attached to the choroid by the lamina suprachoroidea. At the distal end of the ciliary body the inner surface of the sclera protrudes into the sinus of the anterior chamber as the **scleral protuberance,** which is bounded distally by a depression in the substance of the sclera, the **internal scleral sulcus.** The scleral tissue loosens up distally and passes in separate trabeculæ to the sinus of the anterior chamber at the internal scleral sulcus, closing in incompletely the circular **canal of Schlemm,** which is in open connection with the anterior ciliary veins. The trabecular formation joins with similar trabeculæ that rise from the root of the iris to the corneoscleral junction under the name of the **ligamentum pectinatum iridis,** and together they completely fill the sinus of the anterior chamber, or **Fontana's space,** with a loose, spongy tissue.

The sclera, like the cornea, is composed of **flat connective tissue fibers,** but they are not arranged in such regular lamellæ. They assemble into bundles that divide, anastomose, and interlace with each other. The sclera is materially richer in **elastic fibers** than the cornea; they lie on the bundles of connective tissue and are particularly abundant in the inner layers and in the region of the scleral prominence. The sclera contains numerous **cells** that differ in shape from the corneal corpuscles. They have membranelike processes with which they ensheathe the connective tissue fibers and thus resemble tendon cells. Probably the sclera has a system of lymph spaces comparable to that of the cornea in open connection with it and with the spaces of the sinus of the anterior chamber.

i. The Vitreous

The lenticular sac, when it has just separated from the ectoderm, nearly fills the entire cavity of the optic vesicle, leaving only a narrow cleft between it and the distal layer of the latter. This cleft is filled with an extremely fine network of fibrils that come from both the cells of the distal retinal layer and the lenticular epithelium, the **primitive vitreous.** The formation of fibrils encroaches also upon the opposing epidermis cells of the lenticular sac, and fills the space between them. With the closure of the optic cleft and the entrance of the vessels great numbers of mesenchymatous cells enter the gradually widening and deepening cavity of the vitreous, and are reinforced by similar elements that enter from the margin of the vesicle. These mesenchymatous cells also produce fibrils that mingle with the primary ones from the ectoderm and so form the **secondary vitreous.** The **vasa hyaloidea** run in the axis of the embryonal vitreous from the papilla to the lens. The fibrillary network is looser about these than elsewhere in the vitreous. After the absorption of these vessels an axial space remains, the **hyaloid canal.**

The **vitreous** of the adult fills the entire space between the proximal surface of the lens and the retina, and thus occupies by far the greater part of the interior of the eye. It consists of **vitreous tissue** and the **fluid** with which this is saturated. The vitreous tissue is a network of extremely minute **vitreous fibrils,** that are neither collagenous nor elastic, according to their color reactions, but may be classed with the lattice fibers met with in the interior of the lobules of the liver. This network of fibrils contains no cells. Peripherally it condenses into a **limiting layer** that closely adjoins, and is firmly adherent to the membrana limitans interna of the retina. Distally it adjoins first the folds of the orbiculus ciliaris, then the ciliary processes, next the zonula ciliaris, and finally the proximal surface of the lenticular capsule, where it blends with the wall of the **hyaloid canal.** The latter is not a true cavity, but is filled with vitreous tissue that is sharply differentiated from the rest by its far more open structure. As stated above, the limiting membrane blends directly with the membrana limitans interna of the retina; a special structureless membrana hyaloidea does not appear to exist. The vitreous contains only an extremely small number of cells, all of which appear to be wandering cells from the retinal vessels and lie in the limiting layer.

The **vitreous fluid** that saturates the fibrillary network is of alkaline reaction and contains less than 1% of solid constituents, including traces of albumin, a mucoid substance called hyalomucoid, traces of urea, and inorganic salts.

k. The Zonula Ciliaris

The zonula ciliaris, also called the **zonule of Zinn,** and often simply the **zonule,** is a ***system of fibers*** stretched between the ciliary body and the lens that hold the latter in place and is of great importance in effecting the phenomena of accommodation (Pl. 85, Fig. 185). The fibers are not only much stronger than the fibrils of the vitreous, but they also differ from them in their staining reactions, according to which they resemble neuroglia fibers

and the fibrils of Mueller's fibers of the retina. Part of them arise from the surface of the **cells** of the distal layer of the **pars ciliaris retinæ,** part penetrate between them and may be followed proximally to the cells of the orbiculus ciliaris. These pass through the depressions between the ciliary processes to the distal surface of the lens, while those from the distal part of the ciliary body go to the proximal surface, so that the two sets of fibers cross in the region of the equator of the lens, to which special bundles are attached. This sort of attachment renders intelligible what has been said in regard to accommodation. A flattening of the lens must be produced when the zonule is tightened. The interspaces between the fibers of the zonule are filled with aqueous and are in open communication with the posterior chamber.

l. The Blood Vessels of the Eyeball

All of the **arteries of the eyeball** come from the ophthalmic, but are divided into the ***central artery,*** which supplies the optic nerve and the distal portions of the retina, and the **ciliary arteries,** which supply all of the other parts.

The **central artery of the retina** enters the axis of the optic nerve with the vein of the same name about 2 cm from the eyeball and runs in it to the papilla, giving off many branches in the septa of the nerve on the way. In its passage through the lamina cribrosa it anastomoses with Haller's circular arterial plexus and divides in the base of the papilla first into a ***superior*** and an ***inferior retinal artery,*** which immediately divide again into the ***superior temporal, superior nasal, inferior temporal*** and ***inferior nasal arteries.*** The temporal arteries give off first a superior and an inferior macular artery, and then many branches within the layer of nerve fibers as far as the ora serrata, that do not anastomose. Its capillaries do not penetrate beyond the external granular layer. The layer of rods and cones is nonvascular and receives its nutrition the same as the pigment epithelium from the choroid. The central vein of the retina follows the same course as the artery.

The **ciliary vascular system** is divided into a ***proximal*** and a ***distal portion,*** which have many anastomoses. The **proximal part** is fed by the **short posterior ciliary arteries,** running in the immediate vicinity of the optic nerve, which are at first from four to six trunks that divide repeatedly in the neighborhood of the eyeball, pierce the sclera near the optic nerve, and enter the lamina vasculosa choroideæ. On the way they supply the optic nerve and its sheaths with many branches that anastomose with branches of the central artery and form long capillary plexuses about the nerve fibers within the bundles. At their passage through the sclera they give off several branches in the lamina cribrosa that anastomose with branches from the central artery and form **Haller's circular arterial plexus.** The short posterior ciliary arteries supply the entire choroid with blood up to the margin of the orbiculus ciliaris, and here connect with the distal ciliary vascular system through the recurrent arteries. The larger vessels lie externally in the choroid, while the capillaries lie farthest in. Thus the layer of rods and cones of the retina is supplied by the short posterior ciliary arteries, and all of the other layers by the central artery of the retina.

The **distal ciliary vascular system** is fed by both the **long posterior ciliary, and the anterior ciliary arteries.** The former run with the preceding, one to the temporal, the other to the nasal side, pierce the sclera with them and pass distally between the sclera and the choroid. Arriving at the ciliary body they receive the recurrent branches of the short posterior ciliary arteries and then sink into the **circulus arteriosus iridis major,** a circular plexus at the root of the iris which gives off arteries to the iris and to the ciliary body. The former radiate in numerous twigs in the stroma of the iris as far as the margin of the pupillary part, forming many anastomoses with their neighbors on the way. At this margin a second circular plexus is formed, the **circulus arteriosus iridis minor,** from which twigs radiate again toward the pupil. The capillaries of the stroma and muscles of the iris come from this plexus. The arteries in the ciliary body form an extensive plexus from which capillaries branch to twine about the muscle fibers.

The **anterior ciliary arteries** come from those of the ocular muscles and pass through the sclera in the region of the orbiculus. They give off first the proximally running episcleral vessels which enter the sclera, branch in it, and anastomose with the posterior ciliary arteries. Then they give off the conjunctival arteries, which pass forward to the margin of the cornea, where they bend back so as to form loops. After they have given off these branches the arteries perforate the sclera obliquely proximally to the canal of Schlemm and sink into the circulus arteriosus major.

The **ciliary veins** are less distinctly divided into a proximal and a distal system. The main part of the venous blood is carried away by the **venæ vorticosæ.** The larger veins of the lamina vasculosa choroideæ in each quadrant radiate to a point in the region of the equator where they unite into a large venous trunk, the vena vorticosa, of which the eyeball contains four, frequently five. They pass through the sclera and receive the scleral blood from the episcleral veins. The **anterior ciliary veins** correspond in their course to the distal ciliary arteries and receive the venous blood from the conjunctiva bulbi, as well as a part of that from the ciliary body and iris, most of which goes to the venæ vorticosæ. The anterior ciliary veins are also in open connection with **Schlemm's canal,** but this is never filled with blood. The veins corresponding to the short posterior ciliary arteries are developed very poorly.

m. The Lymphatics of the Eyeball

Like the brain the eyeball contains no closed lymphatics lined with epithelium, but has in place of them a ***system of lymph canals in the cornea and sclera,*** which is in open connection with the lymphatics of the conjunctiva. It has also the **perichoroidal space,** situated within the lamina suprachoroidea, that communicates with the subdural and subarachnoidal spaces of the sheath of the optic nerve, by means of which a communication exists between the two eyes. Finally the large chambers within the globe are to be included among the lymph spaces. The **anterior chamber** is in open communication with the **posterior;** both are filled with **aqueous,** an alkaline fluid that has a composition similar to that of the vitreous fluid. The aqueous is secreted by the nonpigmented cells of the pars ciliaris retinæ, and flows away for the

most part through the sinus of the anterior chamber and the canal of Schlemm into the anterior ciliary veins. A part is diffused through Descemet's membrane into the proximal layers of the cornea, and another part is taken up by the veins of the iris.

n. The Nerves of the Eyeball

The nerves of the eyeball, aside from the optic, are the **short ciliary** from the ciliary ganglion, and the **long ciliary** from the nasociliary, comprising in all seven or eight slender nerve filaments that approach the eyeball as both medullated and nonmedullated fibers. They perforate the sclera in the vicinity of the optic nerve, pass forward between it and the choroid, and enter the **plexus of the ciliary body.** On the way they give off branches to the choroid, sclera and cornea.

The **nerves of the choroid** accompany the blood vessels and are for the most part nonmedullated. They form a very wide meshed plexus within the lamina vasculosa, in which little ganglia are imbedded. All of the nerves terminate on the vessels.

The **nerves of the sclera** almost without exception accompany the vessels and are chiefly vasomotor, yet fibers are also found that end free between the bundles of connective tissue.

The **nerves of the cornea,** about forty in number, pass distally from the ciliary nerves to the region of Schlemm's canal, where they form the circular **plexus annularis.** About sixty little nerve trunks radiate from this toward the cornea, lose their medullary sheaths, and enter the substantia propria. By continuously dividing and anastomosing they form here an extensive **basal plexus,** which sends out little stems to the epithelium and the basal substance. The nerves to the epithelium divide repeatedly and pass obliquely through the superficial layers of the basal substance and Bowman's membrane to form on the distal surface of the latter the very close meshed **subepithelial plexus,** from which fibrils enter between the epithelial cells, ramify, and have free ends. The branches of the basal plexus destined for the substantia propria end in little platelike expansions with which they often coapt the corneal corpuscles.

The **plexus of the ciliary body,** or **plexus gangliosus ciliaris,** lies partly on the outer surface of the ciliary body, partly between its bundles and consists of both medullated and nonmedullated fibers with numerous nerve cells. Fibers proceed from this plexus which end free in arborizations between the muscular fibers, as well as others that end with little nodules on these fibers, and still others that end in a similar manner on the muscles of the vessels.

The **nerves of the iris** come from the same plexus and form another one which is wide meshed in the ciliary part, close meshed toward the pupil, and contains no ganglia. Fibers proceed from this to end in the same way as those of the ciliary body on the muscles and vessels of the iris.

o. The Eyelids and the Conjunctiva

The eyelids appear in the second fetal month as low, oval **folds of skin** about the cornea. They remain low at the inner and outer angles, while the

parts between these points grow very rapidly, so that at first a biconvex and later a slitlike palpebral fissure is formed which is completely closed in the third month by an adhesion of the margins of the lids. We have then on the distal side of the cornea a fissure-shaped cavity closed by the lids, the **conjunctival cavity.** This extends laterally for a considerable distance beyond the margin of the cornea and is lined by a mucous membrane called the **conjunctiva,** the epithelium of which consists at an early period of a superficial layer of cylindrical, and one of lower cells which later become several. The conjunctiva begins at the margin of the cornea, covers the distal surface of the sclera as the **conjunctiva bulbi,** then bends about to cover the proximal surface of the lids as the **conjunctiva palpebrarum.** Just before arriving at the point where the lids are adherent the epithelium passes over into the adhering epidermis. A process of cornification begins in the cells of the epidermis in the eighth fetal month which dissolves the adhesion and permits the lids to open. Hairs, and both sweat and sebaceous glands develop from the palpebral epidermis. A line of sebaceous glands grows out from the adherent epithelium of the inner edge of the lids in the third month, which attain a very considerable degree of development, and become known as the **Meibomian glands.** They grow into the connective tissue of the lids and come to lie in a zone of dense connective tissue that supports the central part of each lid and is called the **tarsus.**

The distal surface of the lid of the adult is covered by the **skin,** the general characteristics of which are the same as those of that of the face. The cutis has no papillæ, except at the inner edge, but has a smooth surface next to the epidermis. The subcutis is not very fat, but is very loose, so that the skin of the lid is lifted up into folds very easily. Little woolly hairs, sebaceous follicles and sweat glands are found in it. Next proximally to the subcutis lies the **musculus orbicularis oculi,** the circular, striated fibers of which surround the palpebral fissure. These fibers are assembled into bundles of varying size, grouped to form a single layer that extends over the entire breadth of the lid from its inner edge (Pl. 90, Fig. 193).

The **cilia** project in one or two rows from the outer edge of the lid and arch gently outward. Their follicles penetrate deeply into the layer of the orbicularis and so separate from it the most central portion, neighboring the inner edge of the lid, which is known as the **musculus ciliaris,** or **Riolan's muscle.** Between the cilia lie the **glandulæ ciliares,** or **Moll's glands,** particularly large sweat glands that open together with the sebaceous, into the follicles of the cilia. They have a wider lumen and are not so convoluted as the other sweat glands of the lids.

The **Meibomian glands,** the most prominent formations of the lids, open at the inner edge. They lie in a single row enclosed in the tarsus, and number thirty in the upper, twenty-five in the lower lid. They are from 8 to 10 mm long in the upper lid, and about half as long in the lower. Each gland begins with a single, short excretory duct which is studded with numerous alveoli. The duct is lined with stratified flat epithelium, while the alveoli are filled with polyhedral fatty cells, the most central of which break down and furnish the secretion, the **sebum palpebrale.**

These glands are enclosed in the **tarsus,** a firm plate of densely felted bundles of connective tissue that occupies about the central two thirds of each lid, those of the upper and lower lids being connected at the outer and inner canthi. The tarsus appertains to the conjunctiva, supports the lid, and furnishes a smooth gliding surface for the movements of the latter upon the eyeball. It is separated from the orbicularis by the **fascia palpebralis,** a tight connective tissue into which the tendons of the levator palpebralis superioris and the inferior rectus radiate peripherally. Proximally from these tendons are smooth muscular fibers which originate in the upper lid between the fibers of the levator, in the lower from the connective tissue of the fornix, and are inserted into the peripheral end of the tarsus. These smooth muscles are the **tarsales superior** and **inferior.**

The **conjunctiva palpebrarum** is covered by a **stratified cylindrical epithelium** consisting of a superficial layer of cylindrical, and one or two deep layers of cuboidal cells. It begins a little way from the inner edge of the lid, developing from the gradually thinning epidermis. Many **goblet cells** lie between the cylindrical cells, which are provided with a homogeneous cuticula. The surface of the mucous membrane is perfectly smooth over the entire extent of the tarsus, but toward the fornix it becomes uneven and presents many depressions. The **propria** of the conjunctiva is a firm connective tissue that joins the epithelium closely to the tarsus. Its content of lymphocytes varies in different individuals. In the fornix are to be found **Krause's glands,** or the **glandulæ lacrimale accessoriæ,** the excretory ducts of which open in to fornix conjunctivæ. They resemble the lacrimal glands in their structure.

In the fornix the palpebral passes over into the **conjunctiva bulbi,** which is joined to the sclera by a loose, subconjunctival connective tissue. Both conjunctivæ are practically alike in structure. The epithelium is the same, except that a few millimeters from the margin of the cornea it changes into a high, stratified flat variety, the direct continuation of which is the epithelium of the cornea. Not rarely it contains pigment granules.

The **plica semilunaris,** a rudiment of the palpebra tertia found in many animals, is a fold of the conjunctiva bulbi and has the same structure. Under certain circumstances a little plate of cartilage may appear in its propria. The **caruncula lacrimalis,** situated to its nasal side, has its top covered with stratified flat epithelium which changes on its sides to that of the conjunctiva. It contains sebaceous and sweat glands and frequently little hairs.

The **arteries** of the eyelids, the median and lateral palpebral, form in each lid two vascular arches by anastomosis, the **arcus palpebralis externus and internus.** The former lies in front of the peripheral margin of the tarsus, the latter in the region of the ciliary muscle. The two arches anastomose frequently through pretarsal branches and send twigs to the cutaneous and conjunctival parts. The conjunctiva has beneath its epithelium a very close meshed plexus of very varicose capillaries. The **veins** form a conjunctival and a cutaneous plexus. The former receives the blood from the conjunctiva and pours it into the muscle veins. The cutaneous plexus carries off most of the blood and empties into the superficial temporal and the angular veins.

The **lymphatics** of the lids form a closed system that follows the course of the arteries and is divided into a deep and a superficial portion. The efferent passages open laterally into the parotid, medially into the mandibular lymphatic glands.

The **nerves** of the eyelids, containing sensory and motor fibers, come from various sources that lead back to the ophthalmic, maxillary and facial. They form a pretarsal plexus that is particularly well developed in the region of the free margin of the lid. Numerous fibers from this penetrate the tarsus, twine about the Meibomian glands, and form a second plexus in the propria of the conjunctiva. Other fibers run to the muscular bundles of the orbicularis, and to the cutis, where they form another plexus, the fibers from which end on the muscle fibers and the glands, penetrate into the epithelium, or terminate in end clubs. Such a terminal apparatus as the latter is chiefly to be found in the conjunctiva bulbi, and at the free margin of the lid just beneath the epithelium.

p. The Lacrimal Glands

The lacrimal glands develop in the third fetal month as solid cellular cords growing out from the **epithelium of the fornix,** which soon ramify very abundantly, become hollow, and form two separate glands in such a way that the excretory duct of the upper is surrounded by the ramifications of the lower. At birth the glands are fully developed, but they do not begin to secrete until the third month of life.

The secretion of the lacrimal glands, the **tears,** is a limpid, alkaline fluid having a distinctly salty taste due to the presence of from 1 to 3% of sodium chloride. It also contains about 0.5% of albumin.

The lacrimal are **compound branched tubular glands** with from eight to twelve excretory ducts that open in the temporal part of the fornix. The parenchyma of the gland is divided into many large and small lobules by septa from the connective tissue capsule. The **excretory ducts** are lined with **stratified cylindrical epithelium** formed of an inner layer of cylindrical cells, an outer layer of cuboidal, and a homogeneous membrana propria. Having entered the gland the ducts branch many times in the interlobular connective tissue, both layers of cells continuously decrease in height, and the lumen becomes very narrow. After entrance into the primary lobules the interlobular ducts divide into the **secretory tubules.** These latter also have a **bilaminate epithelium,** though the outer cells are quite flat, branched, and force themselves between the membrana propria and the secretory cells. Probably these are **contractile cells,** similar to those found in the sweat glands, which are phylogenetically related to the lacrimal. The **secretory cells** are partly **cylindrical,** partly **cuboidal.** They contain secretory granules, like those of the albumin secreting glands, and two central bodies near the lumen. The basal part of the cell is free from secretory granules and contains fibrillary radiating mitochondria from which the secretory granules are produced. The cells also contain minute drops of fat. The spherical nucleus lies near the base. Secretory capillaries appear between the cells.

Branches of the lacrimal **arteries** enter the lobules and twine about the

tubules and ducts with their capillaries. The veins empty into the ophthalmic, or those of the muscles.

The **nerves** of the lacrimal gland come from the lacrimal, most of the branches of which only pass through its substance. Those that supply the tubules are nonmedullated and form one plexus on the membrana propria, another at the bases of the secretory cells, from the latter of which fibrils enter and terminate between the cells.

q. The Lacrimal Passages

The formation of the lacrimal passages proceeds from the **nasolacrimal groove** produced by the union of the lateral nasal and maxillary processes. From this a solid epithelial ridge separates itself and produces an **epithelial cord** that grows forward on one side toward the nasal cavity, and bifurcates on the other toward the median periphery of the circular fold of the eyelids which appears at this time. Both branches reach the margins of the lids in the third month, but the trunk arrives at the epithelium of the nasal cavity considerably later. The canalization of the solid epithelial rudiment begins in the early part of the fourth month at the place where the canaliculi are given off, and progresses from this point toward both the nose and the lids.

The **mucous membrane of the canaliculi** is covered by a thick **stratified flat epithelium** resting on a **propria** that is rich in elastic fibers. Between the two is a homogeneous membrana propria. The striated muscular fibers, which are circular about the vertical part and longitudinal along the horizontal, appertain to the orbicularis oculi.

The **mucous membrane of the lacrimal sac** and of the **nasolacrimal duct** is on the contrary covered with a **stratiform epithelium** which is practically the same as that of the respiratory nasal mucous membrane, except that cilia are absent in places, and that goblet cells are met with less frequently. The **propria** also has the character of that of the respiratory mucous membrane, as it is infiltrated with many **lymphocytes.** Little **follicles** are formed in many places, but **glands** like the glanduale nasales appear only in its lower part.

The **arteries** of the lacrimal passages come partly from the median palpebral, partly from the dorsalis nasi and angularis, and form a subepithelial capillary plexus. The **veins** have relations in the nasolacrimal duct that are quite similar to those in many parts of the nasal cavity. They form deep seated plexuses that present the characteristics of **erectile tissue.**

r. The Extrinsic Ocular Muscles

The muscles that serve to move the eye are composed, like those of the body and limbs, of **striated muscular fibers,** but differ from them in a few points. In the first place the fibers are considerably more **slender.** (Pl. 68, Fig. 159). This is particularly the case with the peripheral fibers of each muscle. Furthermore many of the **fibers** of these muscles are **rich in protoplasm.** The nuclei also are not so very peripheral as in the fibers of other muscles.

The extrinsic ocular muscles are supplied very abundantly with **sensory**

nerves that accompany the muscular fibers for long distances and end on them with fine nodules and plates (Pl. 71, Fig. 163). There are also fibers that wind about the muscle fibers like bands and give off numerous lateral twigs and plates. The conditions here are therefore similar to those of the sensory fibers of the muscle spindles, which are not to be found in human ocular muscles. Tendon spindles are likewise lacking. The motor endings do not differ from those of other muscles.

2. THE EAR

a. The Internal Ear

The first sign of the ear appears in the human embryo in about the third fetal week as a roundish spot of thickened epithelium situated laterally from the posterior cerebral vesicle, known as the **ear plate.** Quite similarly to the later appearing rudiment of the lens, the center of the plate sinks in, causing it to take the shape of a cup, and this **auditory cup** is closed in about the beginning of the fourth week to form the **auditory vesicle.** The latter lies close to the hind brain and consists of a low cylindrical epithelium that is higher on the median wall. Rostrally to this median wall lies a **ganglion** from which fibers advance to the wall very soon, while a great part of the undifferentiated epithelium here is transformed into **neuroepithelium.** A duct grows out from the dorsal part of the now somewhat elongating vesicle that closely approximates the hind brain, the **ductus endolymphaticus.** The portion lying dorsally from its mouth we call the pars dorsalis, the rest the pars ventralis of the auditory vesicle. A superficial pouch first protrudes dorsally from the **pars dorsalis,** and a similar one laterally a little later. The former, the **vertical pouch,** has at its base a dilatation, the **ampulla,** into which a part of the neuroepithelium enters from the median wall. A similar ampulla is placed at the rostral end of the second, horizontal pouch, so that we have in all **three ampullæ supplied with nerves** in the pars dorsalis. Two corresponding places of the closely approximated epithelial walls fuse in the vertical pouch and become absorbed so as to present two windows as it were with a high pillar between them. Two **semicircular canals** thus originate from one pouch, an **anterior** and a **posterior.** Both start from the remains of the pars dorsalis with a broad base, the **anterior** and **posterior ampullæ,** unite dorsally and open again into the pars dorsalis with a common canal. A similar process takes place in the horizontal pouch, except that only one window is formed, and therefore only one **horizontal semicircular canal.** The two vertical semicircular canals are at first in the same plane, but later they become perpendicular to each other, revolving as it were about the common canal as an axis. We have now three approximately semicircular canals in the three planes of space that start from the pars dorsalis with five openings, three of which are dilated into ampullæ, while two are not. The ductus endolymphaticus runs along the median surface of the common canal and is dilated at its distal end into the **saccus endolymphaticus.**

The transformations of the **pars ventralis,** part of which are taking place at the same time, are as follows. This portion grows forward ventrally, be-

comes narrowed and bends off toward the rostrum. This bent part is called the **cochlear process.** Its proximal segment swells out and takes a position against the remains of the pars dorsalis, from which the semicircular canals always rise more sharply. The originally median area of epithelium supplied by nerves splits up again, one part going to the remains of the pars dorsalis, which we now call the **utriculus,** a second to the saclike dilatation of the proximal part of the canal of the cochlea, the **sacculus,** and another to this canal of the cochlea itself. Consequently the canal of the cochlea is still more thinned and bends into a spiral as it increases in length. Its initial piece contracts to a short duct, the **canalis reuniens,** connecting with the sacculus.

The mesenchyma in the vicinity of the epithelial auditory vesicle condenses at an early period into a blastema which secretes a **cartilaginous capsule** about the organ, that begins to **ossify** in the fifth fetal month. The original mesenchymatous tissue remains preserved between the cartilage and the epithelial wall, first produces a **membrana propria** about the epithelium and then liquefies for the most part, giving rise to the **perilymphatic spaces** interposed between the membranous and the bony labyrinth on the lateral side. The bony labyrinth has on the whole the same form as the membranous, but encloses the sacculus and the utriculus with a common capsule, the bony vestibule, from which pass on one side the bony semicircular canals, on the other the bony cochlea.

The nasal layer of the membranous labyrinth, leaving out the cochlea, forms a **membrana propria** that is only 4 or 5 μ thick in most places, but attains a thickness of 100 to 200 μ at the places where the nerves end. It is structureless, or presents only a very slight striation, and contains a varying number of stellate cells that anastomose through their processes. It is adjoined externally by connective tissue, the fibers of which unite with the periosteum and pass through the perilymphatic spaces. Internally the membrana propria is covered by an **epithelium** that consists of a single layer of quite **flat, polygonal cells,** except at the places where the nerves terminate. It is only in the **raphe** of the semicircular canals that the epithelium is a low cylindrical (Pl. 91, Fig. 194).

Excluding the cochlea we have five ***terminal places for the nerves,*** a **crista acustica** in each ampulla, a **macula acustica** in the utriculus and in the sacculus, and a **macula neglecta** in the former. The **maculæ** are flat, platelike thickenings of the wall of the labyrinth in which the membrana propria is involved to an even greater extent than the epithelium. The **cristæ** are crescentic ridges protruding into the lumen of the ampullæ that have on section the form of a cone. The crest is formed from the greatly thickened membrana propria, which presents externally a furrow corresponding to the crest, the **sulcus transversus.** Internally the crest is covered by **neuroepithelium,** which changes gradually on its sides into flat epithelium. The two thickened ends of the crest are surrounded by a zone of simple cylindrical epithelium, the planum semilunatum (Pl. 91, Fig. 194).

The **sinus epithelium,** or **neuroepithelium** of the maculæ and cristæ is stratiform and consists of two kinds of cells, ***hair*** and ***stay cells.*** The **hair cells** lie a little distance apart, forming a single layer on the epithelial

surface. Each is bottle-shaped, 25 to 40 μ long, and extends down with its basal end to about the middle of the epithelium. Its nucleus is large, spherical, has a well-developed framework of chromatin and a nucleolus, and lies near the base of the cell. Two central bodies are found near the surface. The latter is covered by a cuticularized plate from which a number of fine **auditory hairs** extend. It is difficult to determine the length of these as they do not run out freely. On the cristæ they enter into the formation known as the **cupula terminalis,** which looks in a cross section like a cylindrical hat resting on the crista (Pl. 91, Fig. 194), and exhibits a very distinct longitudinal striation. Views differ as to its morphological interpretation. On the maculæ the auditory hairs very soon bend at a right angle, lie close together, and form the abutments of the **otoliths,** crystals of carbonate of lime up to 10 μ long, that are held together by a sort of membrane. The **stay cells** lie between the hair cells, their bodies resting on the base of the epithelium, their nuclei forming two or three rows. Each cell sends a slender process toward the lumen, which reaches the surface between the hair cells.

The **nerves** coming to the maculæ and cristæ are the peripheral processes of the bipolar cells of the **intumescentia ganglioformis** of the internal auditory meatus (Pl. 91, Fig. 194; Pl. 29, Fig. 75). They lose their medullary sheaths as they pass through the membrana propria and form a plexus beneath the epithelium, from which fibers enter the latter, where they run between the hair cells and the bodies of the supporting cells and then turn toward the bases of the latter. Each fiber forms a sort of terminal bowl into which a hair cell is set like an acorn in its cup. A fiber often divides into several twigs, each of which receives the base of a hair cell in its terminal cup. A great number of fibrils radiate from the terminal cup, are studded with varicosities, and join closely to the protoplasm of the hair cells.

The **membranous cochlea** needs a separate description because its structure is so complex. It is a closed duct, the **ductus cochlearis,** blind at both ends, which begins in the bony vestibule with the **vestibular blind sac,** rises within the bony cochlea in a spiral of two and a half to two and three quarters turns, and terminates with the **blind sac of the cupola.** The very narrow, frequently obliterated, **canalis reuniens,** or **Hensen's canal,** coming from the sacculus, opens into the ductus cochlearis distally from the short, blind sac of the cupola. The ductus cochlearis is triangular on cross section (Pl. 91, Figs. 194 and 195). If we think of the cochlea as standing upright, although in fact it lies horizontally, and this applies to all that follows, the section of the cochlear duct forms a nearly right angled triangle, the vertical cathetus of which is not a straight line, but one that is curved outward. The ductus cochlearis touches the capsule of the cochlea with this vertical cathetus. The horizontal cathetus extends from the bony outer wall to the lamina spiralis ossa of the modiolus cochleæ, while the hypotenuse runs obliquely through the bony cochlear duct. There are two cavities, one above the cochlear duct, the **scala vestibuli,** and one beneath it, the **scala tympani.** The latter ascends with the membranous cochlear duct in the bony duct and merges with it in the cupola in the so-called **helicotrema.** The scala tympani ends blind at the ventricular blind sac, being closed in by the membrane of the

fenestrum rotundum. The scala vestibuli on the contrary descends into the large perilymphatic space of the bony vestibule.

If we now turn back to the form of the ductus cochlearis we see that the horizontal cathetus of the triangle is shortest in the base of the cochlea, that it becomes longer as we go up, and that the reverse is true of the vertical cathetus, because the membranous cochlear duct constantly becomes broader and lower toward the apex of the cochlea.

In the initial portion of the vestibular blind sac the horizontal wall, which we now prefer to call the tympanal wall on account of its neighborhood to the scala tympani, has an extremely complicated terminal nerve apparatus, the **papilla spiralis,** or the **organ of Corti.** As a whole this is a spiral epithelial crest that slopes gradually into both the ventricular blind sac and the blind sac of the cupola, falls away abruptly on both sides, gradually broadens from below upward, and attains its greatest thickness in the middle of the cochlea. We will now briefly analyze the separate walls of the canal of the cochlea (Pl. 91, Fig. 195).

The **vestibular wall** separates the ductus cochlearis from the scala vestibuli and is commonly known as **Reissner's membrane.** It extends from the crista Reissneri on the outer wall obliquely inward and downward to the limbus spiralis covering the lamina spiralis ossea. Its composition is that of a double, very thin layer of epithelium. The flat cells blend on the one hand with the epithelium of the scala vestibuli, on the other with that of the limbus spiralis and the outer wall of the ductus cochlearis.

The **outer wall** of the ductus cochlearis is formed by the **ligamentum spirale,** a cushion of connective tissue placed within the cochlear capsule which is crescentic in cross section. It reaches up a little way into the scala vestibuli, while below it covers almost the entire outer wall of the scala tympani. Its inner wall shows three projections, the **crista Reissneri,** from which Reissner's membrane extends, the **crista spiralis,** which serves for the insertion of the tympanal wall of the ductus cochlearis, and a little above this the flat **prominentia spiralis.** The spiral ligament is a much thickened periosteum, but contains a basal substance resembling the membranæ propriæ. In it lie fine connective tissue fibers and numerous stellate or elongated cells with anastomosing processes. All of the connective tissue fibers in the region of the crista spiralis converge toward the latter. The spiral ligament, so far as it lies in the ductus cochlearis, is covered by an epithelium which we may differentiate into two different portions, the **stria vascularis,** reaching from the crista Reissneri to the prominentia spiralis and adjoining the **sulcus spiralis externus,** which leads over into the epithelium of the tympanal wall.

The **stria vascularis** presents a fairly high ***stratified*** epithelium, the superficial cells of which are flat and stain intensively, the deeper ones irregularly cuboidal. The demarcation of the spiral ligament from the connective tissue is less sharp. The characteristic mark of this epithelium is the number of **blood capillaries** it contains just beneath the most superficial layer of cells, because of which the secretion of the endolymph that fills the membranous labyrinth is ascribed to the stria vascularis. Embryology teaches us that the epithelium of the stria is a mixture of epithelial and connective

tissue, the former grown through by the cells of the latter, as we shall soon see in another place.

On the prominentiä spiralis, in the substance of which is a blood vessel, the vas prominens, the epithelium thins into a single layer of flat or cuboidal cells, and blends with that of the **sulcus spiralis externus.** This sulcus encroaches upon the tympanal wall and is but slightly developed in the base of the cochlea because of the shortness of that wall, but gradually attains a considerable breadth. Its epithelium consists of a single layer of **cuboidal** or **cylindrical cells,** between which are long connective tissue cells that reach the surface in the vicinity of the prominentia spiralis.

The **tympanal wall** stretches between the crista spiralis externally and the lamina spiralis ossea internally. The latter is composed of two bony plates, between which a canal leads into the spiral canal and is covered by a plateaulike mass of connective tissue, the **limbus spiralis.** Toward the spindle of the cochlea the limbus slowly blends with the periosteum, in the ductus cochlearis it projects like a hook to form the **sulcus spiralis internus** by an arch convex internally to the lamina spiralis. We may thus distinguish two lips of the limbus, one vestibular, extending freely into the ductus cochlearis, and one tympanal, covering the end of the lamina spiralis ossea and blending with the membrana basilaris about to be described. The structure of the limbus is quite similar to that of the spiral ligament. Its free surface is traversed by radiating furrows that divide it into about twenty-five hundred ridges, the **auditory teeth of Huschke.** These do not appear in sections as the furrows separating them are perfectly leveled by the epithelium covering the limbus. This epithelium blends at the point of the hook with the simple cuboidal epithelium of the sulcus spiralis internus. The organ of Corti lies between the latter and the sulcus spiralis externus.

The tympanal wall of the ductus cochlearis is formed by the **membrana basilaris** which is stretched between the tympanal lip of the limbus spiralis and the crista spiralis. It consists of radiating, flat fibers of connective tissue, the **auditory basilar fibers,** the length of which increases constantly from the base to the apex of the cochlea. They are embedded in a **homogeneous basal substance.** The membrana basilaris is bounded toward the ductus cochlearis by the finely striated, nucleated **border layer,** toward the scala tympani by the **tympanal cover layer,** which consists of several laminæ of elongated, loosely placed cells that blend on each side with the single layer of low cells of the epithelium of the scala tympani. Within this tympanal cover layer may be seen the cross section of the **vas spirale.**

The membrana basilaris serves as vibrating membrane on which the perceptary apparatus of **Corti's organ** is constructed, grouped into two peculiar lines of **pillars.** These pillars are long, slender, cuticular formations that start from the membrana basilaris with broad bases, taper, and then swell out again into a knob. They stand with their feet wide apart and with their upper ends leaning against each other, so as to enclose a triangular spiral space that extends to the top of the cochlea, **Corti's tunnel.** Its breadth increases from below upward, the same as the length of the basilar fibers. The **pillars** are known as the ***outer*** and the ***inner.*** The **outer pillars** are longer and slant more

than the inner. Each outer pillar ends above in a roundish **head** that is prolonged outward in a narrow **head-plate.** The **inner pillars** are shorter and stand more nearly upright. They also have knoblike swellings above, but each furnishes a sort of **socket** in which the head of an outer pillar is received, so as to form a jointlike articulation. The head of the inner pillar is prolonged outward in a **phalangeal process** that covers the head of the outer pillar and closely adjoins the beginning of its headplate. The inner pillars are more slender than the outer, and number six thousand to forty-five hundred of the latter, so one outer pillar often has to articulate with two inner pillars.

The pillars are cuticular formations secreted by the **pillar cells** or **basilar cells,** the remains of which we may still see forming a protoplasmic coat to Corti's tunnel containing a row of nuclei at the foot of each pillar. Fine supporting fibrils pass through the homogeneous substance of the pillars and form a dense bundle in the middle portion, from which they radiate like a fan into the feet and heads.

The other parts of the organ lie inside and outside of the framework formed by the pillars. The **inner division of Corti's organ** consists of a single row of **inner hair cells.** These are bulging or cylindrical cells with rounded bases that occupy only a little more than half the thickness of the epithelium. The longitudinal axis of each is parallel to that of the inner pillar. The large, spherical nucleus lies at the base of the cell, the protoplasm is very clear and shows between the nucleus and the base a granular thickening, **Retzius's body,** as well as a more filamentous thickening in the upper end, **Hensen's body.** The cell has a cuticularized **cover plate** on its free surface, from which extend ten or twelve short, thick **auditory hairs.** The space beneath the inner hair cells is filled by two high cylindrical cells, the outer of which is known as the **inner phalangeal cell,** the inner as the **border cell.** They hold the inner auditory cell between them and each sends to the surface of the epithelium a long process that has a little cuticularized plate lying at the same level with the cover plate of the inner hair cell and the headplate of the inner pillar. Farther inward the epithelium of Corti's organ suddenly declines and blends with that of the sulcus spiralis internus.

The **outer division of Corti's organ** is attached to the outer pillar, and has in general the same structure as the inner, except that instead of one, there are *three or four rows of hair cells.* Consequently, there are three or four times as many outer hair cells as inner, 12,000 of the one to 3,300 of the other. Each hair cell is separated from its neighbor by a **supporting cell,** here called a **Deiter's cell.** The outer hair cells have the same structure as the inner, and differ only in being rather longer, more slender, and less bulging. Between the first outer hair cells and the outer pillar is an open space, called **Nuel's space.** The supporting cells are long and cylindrical. The upper ends of their bodies grasp each the base of a hair cell and extend out in a slender process between two neighboring hair cells to the surface of the epithelium, where a knucklelike **headplate** articulates with it between the covers of the hair cells. The last supporting cell, the third outer, is particularly strong, and has a long process that is bent inward.

On the other side of this the epithelium again slopes away abruptly and blends with that of the sulcus spiralis externus. Each outer supporting cell has a bundle of fibrils passing through its longitudinal axis, part of which radiate out in a fanlike manner beneath the base of the hair cell, while part continue into the process. The nuclei of the supporting cells lie deeper than those of the hair cells.

The cuticularized plates of the inner and outer supporting cells are movably connected with the headplates of the outer and the phalangeal processes of the inner pillars. Thus there is formed on the surface of the organ of Corti a membrane composed of separate pieces movable upon one another, which extends from the border cell on the inner side to the last supporting cell on the outer, is known as the **membrana reticularis,** and presents roundish apertures in which the hair cells with their cover plates are so inserted that no one touches another.

The **nerves** entering the organ of Corti come from the **spiral ganglia,** which fills the spiral canal as a coherent mass. Like the intumescentia ganglioformis, it is composed of **bipolar cells,** the peripheral processes of which are invested with medullary sheaths, and penetrate between the two layers of the lamina spiralis ossea to Corti's organ, which they enter through apertures in the basilar membrane, the **foramina nervina.** As they pass through these apertures the fibers lose their medullary sheaths and divide into two cords, one of which runs directly upward to the inner hair cells, while the other crosses Corti's tunnel and forms a plexus between the outer supporting cells, from which fibers rise to the bases of the hair cells, where they behave just the same as those of the maculæ and cristæ.

The **membrana tectoria,** or **Corti's membrane,** forms a bridge over the sulcus spiralis internus from the limbus spiralis. It lies first as a thin cuticula on the epithelium of the limbus, then thickens greatly over the sulcus spiralis internus, thins again, and bends about like a hook, to end at the last supporting cells. It has a fine parallel striation, is cuticular in nature, and consequently contains no nuclei. Its position is not always the same; sometimes it lies close to Corti's organ, sometimes at quite a distance, and probably acts as a muffler.

The **arteries** of the membranous internal ear come principally from the internal auditory through the vestibular, vestibulo-cochlearis, and cochlearis. The first supplies the utricle, semicircular canals, and saccule, the last the cochlea, while the second sends its blood into both regions. The branches pass with the nerves to the membranous labyrinth, where they ramify on its outer surface and in the membrana propria. The plexuses in the latter are particularly abundant beneath the nerve endings. In the cochlea the arteries run out from the modiolus into the bony intermediate wall and enter the periosteum of the scalæ, the ligamentum spirale, the stria vascularis, and the limbus spiralis, but do not penetrate any farther into Corti's organ. The **venous blood** of the cochlea gathers into the vena spiralis modioli. The vas spirale is probably one of the root veins and is connected with them by branches radiating between the leaves of the lamina spiralis ossea. The rest of the venous blood of the membranous labyrinth is carried away by the venæ

aqueductus vestibuli and aqueductus cochleæ, the latter of which also takes a part of the blood from the cochlea.

The cavities of the internal ear are lymph spaces. The membranous labyrinth is a cavity that is completely closed in on all sides, does not communicate with the outer world, and is filled with **endolymph,** a limpid, alkaline fluid which contains traces of albumin, mucin and salts. No change of this fluid has been demonstrated. The cavity of the membranous labyrinth communicates through the **ductus endolymphaticus** with the **saccus endolymphaticus** situated within the skull between the two layers of the dura. Under normal conditions it contains only very slight traces of endolymph.

The **perilymphatic spaces,** that surround all parts of the membranous labyrinth, are particularly well developed in the bony vestibule, laterally from the saccule, where they form the **cisterna perilymphatica,** into which the perilymphatic spaces of the semicircular canals and of the scala vestibuli empty. These perilymphatic spaces are not closed like the endolymphatic, but are in open communication with the lymph spaces about the bulb of the jugular vein through the **ductus perilymphaticus,** which starts from the initial portion of the scala tympani.

The composition of the **perilymph** is the same as that of the endolymph, except that it is richer in organic constituents.

b. The Middle Ear

The **middle ear,** or **tympanic cavity,** is a diverticulum of the ***first*** entodermal ***pharyngeal pouch,*** which appears about the end of the first fetal month as a narrow, prismatic cavity. From it comes by lateral growth and contraction of its median portion the **tubotympanal canal,** which is partially occluded for a time by adhesion of its epithelium. Dorsally from this lie the **auditory ossicles,** developing from the second pharyngeal arch and the cartilaginous capsule of the labyrinth, and surrounded by an embryonal gelatinous tissue. As the latter disappears the tubotympanal space advances and surrounds the auditory ossicles, so that finally these, covered with epithelium, come to lie in the space now called the **tympanum,** or **drum.** The portion of the tubotympanal space connecting the tympanum with the pharynx is drawn out by a marked longitudinal growth into the narrow **tubal canal,** or Eustachian tube, in the median and dorsal walls of which cartilage develops in the fourth month.

The **mucous membrane of the middle ear** covers all the structures in this cavity and blends medially with the mucous membrane of the Eustachian tube, laterally with that of the tympanic membrane. The **epithelium** has a ***single layer of cells*** that are generally high cuboidal in the recesses and depressions, and flatter on the ossicles and the promontory. The cells are ciliated in the depressions, particularly on the floor of the tympanum and in the sinus tympani. The epithelium rests on a dense connective tissue **propria,** which passes directly into the periosteum. There is no submucosa, and no glands are to be found in the tympanum.

At the ostium tympanicum this passes over into the thicker **mucous membrane of the tube,** which is connected first with the bone and then

with the cartilage by a connective tissue submucosa, and forms longitudinal folds, especially along the floor of the tube. The **epithelium** is a continuation of that of the nasopharynx, **stratiform** and **ciliated,** in which many goblet cells may be found. The **propria** is thin and contains many **lymphocytes,** which become the more numerous the nearer we approach the ostium pharyngeum. Here, also, are **lymph follicles,** that project into the submucosa and constitute as a whole the **tonsil of the Eustachian tube.** In the propria and submucosa of the median wall of the cartilaginous tube are **mucous glands** that form a thick layer toward the pharynx. The hook-shaped **cartilage** lies mainly in the median wall and roof of the tube, and encroaches but little on its lateral wall. At birth it consists of hyaline cartilage, but networks of elastic fibers develop in its basal substance later.

There is very little to say about the **ossicles** from a histological standpoint. They contain a little medulla and are otherwise composed of compact bone substance. Their articular ends are provided with cartilages. The manubrium has a cartilaginous coat which is complete in its distal part, but proximally is confined to its lateral edge. A meniscus of cartilage is interpolated in each of the joints between the ossicles. The margin of the foot plate of the stapes is covered with cartilage, as is also the ora fenestræ ovalis, while the annular ligament of connective tissue forms the junction between the two cartilages and allows the stapes only a limited movement.

The two **muscles of the middle ear** consist of **striated muscular fibers,** some of which are very fine, some coarser. The stapedius is very rich in interfascicular connective tissue. The stapedius is innervated by the facial nerve, the tensor tympani by the trigeminus. The structure of the motor end plates is typical. Apparently muscle and tendon spindles are to be found in them.

The **arteries** of the middle ear come from various sources, the stylomastoid, middle meningeal, ascending pharyngeal, internal carotid, and tympanic, which furnish a very abundant supply of blood to the tympanum. The larger branches run in the periosteum and form a rather dense capillary plexus in the propria. Many direct arteriovenous anastomoses also appear to exist. The **venous blood** flows away in the pterygoid plexus, the middle meningeal, and the deep auricular veins.

The **lymphatics** form a plexus in the propria of the mucous membrane and empty into the inferior auricular glands.

The **nerves** of the tympanum come from the tympanic plexus in the periosteum of the promontory, which is formed from the medullated branches of the tympanic nerve. The plexus is also supplied with medullated fibers through the ramus anastomoticus nervi facialis, and with nonmedullated through the nervi carotico-tympani. It is plentifully furnished with ganglia and sends the minor superficial petrosal nerve to the otic ganglion, as well as numerous branches to the tympanic mucous membrane. The latter form a subepithelial network from which twigs enter between the epithelial cells, and also a branch is sent to the mucous membrane of the Eustachian tube.

c. The External Ear

The **external ear** originates from the middle portion of the **first pharyngeal sulcus,** which does not form a cleft in man, any more than any of the other four. It deepens and is surrounded by six little **aural eminences,** three of which appertain to the first visceral arch, and three to the second. While these blend with the **free aural fold** surrounding them caudally to form the **pinna,** the concha sinks in deeply toward the end of the second fetal month and forms a passage lined with epithelium, the **primitive external auditory meatus,** at the end of which is formed the roundish epithelial **external auditory plate,** which lies to the medial side of the cartilaginous rudiment of the handle of the malleus. The tympanum grows against it from the dorsal side and shoves it medially. After the lumen of the external auditory meatus has split into two leaves the external auditory plate, the meatus becomes closed off from the tympanum by a deeply situated almost horizontal membrane embracing the handle of the malleus, the **tympanic** or **drum membrane.** A reticular cartilage develops in the primary part of the meatus and in the pinna, while in the secondary part formed by the splitting of the external auditory plate the bony auditory meatus comes to lie in postembryonal life, developed from the tympanic ring and the adjoining parts of the temporal bone.

Three parts of the adult **membrana tympani** may be differentiated from without inward, the ***pars cutanea,*** the ***substantia propria,*** and the ***pars mucosa.*** The **substantia propria** forms the basis of the membrane and consists of connective tissue **drum membrane fibers** which blend with the **annulus tendineus,** composed of connective tissue reinforced by elastic fibers that peripherally fills the sulcus tympanicus of the tympanic ring. The fibers of the drum membrane are united into flat bundles that form two layers. The inner bundles radiate from the annulus tendineus to the umbo, or the stria malleolaris; the outer, on the contrary, run in circles with the umbo as a center. The union of the handle of the malleus with the drum membrane is effected mainly by the fibers of the inner layer which form loops about it. But this regular arrangement of the bundles of connective tissue is found only in the region of the membrana tensa, for in the membrana flaccida the cutaneous and mucous parts are separated by a loose connective tissue that appertains to the cutis. Between the bundles of connective tissue are stellate connective tissue cells, the processes of which anastomose.

The **pars mucosa** is covered by a **single layer of the epithelium of the tympanic cavity,** which here is very low, has no cilia, and rests on a quite thin connective tissue **propria** that is joined to the substantia propria.

The **pars cutanea** is identical with the skin of the external auditory meatus.

The **external auditory meatus** is lined with skin. The **epidermis** is relatively thin and exhibits distinct cornification everywhere. The thickness of the **corium** varies in different places. Papillæ are poorly developed and entirely absent in the cutaneous coat of the membrana tensa of the drum membrane. A **subcutaneous connective tissue** with fat cells is developed only in the cartilaginous portion of the meatus, in the bony portion the corium

blends directly with the periosteum. With the exception of the part covering the drum membrane the skin of the meatus contains **hairs,** and both **sebaceous** and **ceruminous glands.** The latter are metamorphosed sweat glands and empty in infants through narrow openings into the distal parts of the hair follicles, but in adults they wind like corkscrews through the epidermis and their rather funnel-shaped mouths come to lie near the hair follicles. In their structure they exactly resemble the sweat glands of the skin, except that they are usually much larger, their bodies are more convoluted, and the lumens of their tubes are larger. The simple glandular tube also is not rarely divided, and then we have to deal with branched tubular glands.

The **cerumen** is a whitish, yellowish, or in many races brownish, waxlike substance secreted by the sebaceous and ceruminous glands, the latter furnishing the softening fluid only. It contains minute drops of fat, pigment granules, desquamated epithelium, and hairs.

The **cartilages of the external auditory canal** are **reticular,** and are enclosed in a perichondrium rich in elastic fibers.

The **pinna** is covered by a thin **epidermis,** beneath which is a thin **corium** with poorly developed papillæ. The **subcutaneous tissue** is better developed on the medial than on the lateral surface, so that the skin is more easily movable on the former. It is permeated in the lobule with fat cells. **Minute hairs** and **sebaceous glands** are present everywhere in the skin of the pinna. **Sweat glands** are found mainly in the lobule, on the distal surface of the antitragus, and on the eminentia scaphæ. The **cartilages** supporting the auricle have the same structure as those of the external auditory meatus.

The **arteries** of the meatus and of the pars cutanea of the drum membrane come from the superficial temporal and the tympanic. They form a dense capillary plexus in the cutis through radially entering arterial twigs together with a larger branch beneath them in the stria malleolaris, known as the malleolar artery. A similar plexus in formed from the vessels of the tympanic cavity in the propria of the pars mucosa of the drum membrane, and these two plexuses anastomose. The **veins** follow the course of the arteries, form a marginal plexus in the drum membrane, and flow into the external jugular and the internal maxillary veins, and into the pterygoid plexus. The arteries of the auricle come from the anterior and posterior auricular, and the blood is carried away in veins bearing the same names.

The external ear is supplied with many **lymphatics** that form two dense, anastomosing plexuses in the drum membrane, a cutaneous and a mucous. The efferent vessels accompany the arteries and arrive at the anterior, posterior, and inferior auricular, and the deep cervical glands.

The **nerves** of the pars mucosa of the drum membrane come from the tympanic plexus, those of the rest of the external ear from the auriculo-temporal and the auricular branch of the vagus. They form a dense plexus in the corium of the drum membrane, from which fibers rise into the epidermis and there end free between the cells with arborizations. Other fibers penetrate into the substantia propria and form there a second plexus from which fibers with arborescent endings run between the bundles of connective tissue. The skin

of the auricle is supplied by the auricularis magnus in addition to the auriculotemporal. The motor nerves of the external ear are branches of the facial.

3. THE OLFACTORY ORGAN

The sensations of smell are perceived through the **olfactory epithelium** situated in the **olfactory region** of the nose, which occupies, as we have already learned, only the superior turbinate and the corresponding part of the nasal septum. This characteristic epithelium may be demonstrated in the human embryo at the end of the first embryonal month in the **olfactory fossa.** Its cells send their central processes into the brain, forming the olfactory nerve. The olfactory organ gradually comes to lie in the nasal cavity, but the space occupied by it is always smaller than in many of the lower animals, because **Jacobson's organ,** a protrusion from the median wall of the olfactory fossa covered with olfactory epithelium, undergoes an almost complete involution in man, while it forms a well developed part of the organ in other animals, most of whom have a better sense of smell.

The **olfactory** is a **neuroepithelium** composed of specific, sensory, **olfactory cells and supporting cells.** It is demarked from the respiratory epithelium of the nasal cavity by its yellowish color, and the greater abundance of its nuclei. Its thickness, 60 μ, is only slightly greater (Pl. 92, Fig. 196).

The **olfactory cells** pass through the entire thickness of the epithelium. They are very slender, and their bodies present only circumscribed thickenings at the places where the nuclei are situated, beyond which they quickly become attenuated again and pass into quite slender, often rather tortuous processes that form the **fibers** of the **olfactory nerve.** The body of the olfactory cell rises above the surface of the epithelium in the form of a little vesicle from which six to eight quite short **olfactory hairs** project. The **olfactory vesicle** is developed from the central bodies of the embryonal olfactory cells. Each of the olfactory hairs ends with a little nodule in the wall of the olfactory vesicle.

The **supporting cells** are considerably broader than the olfactory. Their nuclei form the deeper layers of the nuclear stratum, while those of the olfactory cells are situated more superficially. The body is provided with numerous longitudinal grooves for the reception of the olfactory cells, and with many dimples to accommodate the nucleated parts of the latter. It contains granules of a yellowish brown pigment that gives its characteristic color to the olfactory region. The distal end of the cell contains a double central body that usually extends proximally in several feet. Between the latter lie a third kind of cells, the **basal,** which are small and have anastomosing processes.

The surface of the olfactory mucous membrane is covered by a homogeneous layer secreted by the supporting cells that is bounded distally by a fine cuticula into which the vesicles and hairs of the olfactory cells project.

There is no basal membrane in the olfactory region.

The **propria** consists of reticulated tissue in its superficial, of loose connective tissue in its deeper parts. It contains very many **lymphocytes** and some little **lymph follicles.** The adjoining **submucosa** consists of loose

connective tissue and contains many elastic fibers, which are also met with in smaller numbers in the deeper layers of the propria.

The propria contains many **olfactory** or **Bowman's glands** (Pl. 56, Fig. 133). These are of the **branched tubular variety,** with the tubules lined with **cuboidal** or **conical cells** which contain many albuminoid secretory granules, like those of the parotid, and are therefore purely **serous glands.** Several tubules unite to form an excretory duct that very soon dilates like a bladder lined with a single layer of low cuboidal epithelium, to form a reservoir for the secretion. At the margin of the epithelium this bladder contracts into a narrow excretory tube that opens on the surface and is lined throughout its intraepithelial course with similar low cells.

The propria is naturally very rich in **nerve fibers,** for each olfactory cell of the epithelium sends one into it, where they assemble into little bundles. Larger bundles are formed from the smaller ones, lie close to the bone, and run in special grooves to the cribriform plate of the ethmoid, pass through this and enter the **olfactory bulb.** Each bundle is enclosed by a continuation of the dura, and a perineural sheath may be perceived even within the olfactory organ. The fibers that compose these bundles are **nonmedullated** throughout their entire course and are unique, as compared with other nonmedullated fibers, in that they also lack the sheath of Schwann. Having arrived at the olfactory bulb each olfactory fiber enters a **glomerulus olfactorius** and breaks up into a terminal arborization.

In addition to the olfactory fibers the olfactory mucous membrane contains **sensory fibers from the trigeminus** that rise up between the epithelial cells and end free.

4. THE ORGAN OF TASTE

The organs of the sense of taste have been discussed in the description of the epithelium of the surface of the tongue. It was stated there that in adults **taste buds** are to be found in the stratified flat epithelium that covers the lateral surfaces of the circumvallate papillæ and the opposite part of the coronal sulcus. They are found elsewhere in adults only in the epithelium of the circumvallate papillæ, sparingly in the fungiform, in the epithelium of the soft palate, and of the entrance to the larynx, where it has a stratified flat epithelium.

Each bud is barrel-shaped, has an average height of 80 μ, a maximum breadth of 40 μ, and stands with its longitudinal axis always perpendicular to the surface of the epithelium. It rests with its base on the propria and its distal end in the floor of a little opening on the surface of the epithelium, the **taste pore,** surrounded by the cells of the stratified flat epithelium (Pl. 92, Fig. 197).

Three kinds of cells may be distinguished in each taste bud, two of which are **supporting,** the third **sensory.** A number of branching cells lie in the base of each taste bud with their longitudinal axes parallel to the surface and anastomosing with their processes. These are the **basal cells.** From them rise vertically to the surface the second kind of **supporting cells,** which are

long, extend to the floor of the taste pore and have sometimes slender, sometimes bulging cell bodies. Each has at the basal end several short footlike projections that anastomose with the processes of the basal cells, while it tapers at the distal end and forms the floor of the taste pore. Each cell has a fine cuticular edge that projects a little into the pore. The supporting cells are irregularly distributed through the entire inner space of the bud with their nuclei at various levels.

The **sensory** or **taste cells** are long and threadlike, vary in number from four to eight in each bud, pass through the entire thickness of the latter, and are distributed irregularly between the supporting cells. Their basal ends are also connected with the basal cells. Each is very slender and dilates at the site of the nucleus after a longer or shorter course. The nucleus is considerably smaller and stains more darkly than that of the supporting cell. Distally from the nucleus the cell body again becomes slender and now runs to the floor of the taste pore, into which it sends a long process, the **taste rod.** The taste rods converge distally into the pore, but do not quite reach the surface of the epithelium with their ends.

Open spaces are left within the bud between the supporting and the taste cells that are known as **intragemmal spaces.** They communicate with the **subgemmal spaces** between the basal cells, and the **perigemmal spaces** at the surface of the bud.

The **nerve fibers** that supply the taste buds belong to the glossopharyngeus and are therefore the peripheral processes of the unipolar cells of the ganglia superius and petrosum of this nerve. They form an extensive plexus studded with multipolar ganglion cells in the propria beneath the bud, from which come **intergemmal fibers** that branch in the stratified epithelium between the buds, **perigemmal fibers,** which are closely adjacent to the surface of the bud and weave about it, and **intragemmal fibers** in the bud itself. They branch repeatedly, closely adjoin the sensory cells, and extend freely between them.

X. THE SKIN

The entire surface of the human body is covered uniformly by the skin, which consists of two parts, an outer derived from the ***ectoderm,*** the **epidermis,** and an inner from the ***mesenchyma,*** the **cutis.** The **epidermis** in the early stages of embryonal life is an epithelium having two layers, the deeper of which, composed of cuboidal cells, is the **germinal layer,** while the superficial **covering layer,** or **periderm,** is made up of flat cells. The latter exhibits **cornification** at an early period and consists in many places of several superimposed layers. Toward the end of the second month a differentiation of the epidermis sets in, beginning on the ventral and proceeding toward the dorsal surface of the body. The cells of the germinal layer multiply and provide a third layer that is interposed between it and the periderm, the **stratum intermedium,** which is at first single, but soon becomes stratified. While the single layer of cells of the germinal layer now becomes cylindrical, these cells are polyhedral, are joined together by **plasmodesmi** and develop **epithelial fibers** in their exoplasm that run through several cells, passing through these plasmodesmi. **Keratohyaline granules** appear in the deepest layers of the periderm, the cells of which are now stratified, about the end of the third, or the beginning of the fourth fetal month, and render opaque the formerly transparent epidermis. The keratohyalin undergoes a change into **eleidin** in the superimposed layer.

The **cutis** lying beneath the epidermis is of mesodermal origin and shows at first an organization corresponding to that of the myotomes, but this disappears soon. Its gelatinous cells develop collagenous and elastic fibers, and produce a loose connective tissue that soon divides into a superficial **corium** and a deeper **subcutaneous tissue.** The surface of the corium is at first perfectly smooth, but very soon the connective tissue invades as it were the bases of these cells, which now appear fringed or notched, so as to form a very firm connection between the epithelium and the corium. Toward the end of the second fetal month the epidermis sinks into the corium in the form of **ridges,** but it is not until the fifth month that the ridges of epidermis over those of the cutis become visible externally. This formation of ridges begins on the volar surface of the fingers and toes and advances proximally.

The skin serves first as a protective covering for the body, guarding it from loss of heat through the development of fat in its deeper layers, and by the growth of hair. In addition it eliminates harmful products from the body through special glands, and is the seat of the so-called **sense of feeling,** i.e., the perception of touch, temperature, and pain.

The **epidermis** is a **stratified flat epithelium,** the thickness of which varies a great deal in different parts of the body and in different individuals.

It is thinnest on the face, abdomen, thigh, and leg, 50 to 90 μ, and thickest on the plantar surfaces of the feet and toes, 1 to 3 mm (Pl. 93, Fig. 197). Its outer surface is uneven and presents a system of **furrows** that separates quadrangular or more elongated, lozenge-shaped elevations. These furrows and fields appear also at the border of the epidermis and corium as ridges that project into the latter and are connected by numerous cross ridges, so that the detached epidermis, when seen from below, presents a more or less fine network, the **rete Malpighi,** that embraces in its meshes the elevations of the corium. At other places, as on the forehead and the auricle, the reverse is the case; the corium has a network of ridges on its surface into which the epidermis sinks with corresponding elevations. A further complication of this epidermis-corium border is that the ridges of the corium are studded wth secondary elevations, **papillæ,** which project more or less into the epidermis. These are flat and unimportant in the skin of the face, while they may be 200 μ long on the glans penis.

The depressions between the papillæ are filled by the **germinal layer,** or **stratum germinativum,** of the epidermis. This is covered smoothly on the outside by the **horny layer,** or **stratum corneum,** which is usually the thinner, but the difference is very soon equalized as the entire thickness of the epidermis increases, and then the growth of the latter is exclusively through a thickening of the horny layer that may finally attain ten times the thickness of the germinal. The germinal layer may be divided into the following sublayers (Pl. 93, Fig. 198):

1. The **stratum cylindricum,** which consists of a single layer of cylindrical cells of an average height of 15 μ. The nucleus lies in the center of the cell. The proximal surface with which the latter rests on the corium exhibits a fine indentation with the connective tissue of the corium interlocking into the intermediate spaces. The cells of this layer are separated from one another and from the distal layer by fine **intercellular spaces** that are traversed by **cell bridges,** so that the stratum cylindricum and the next distal stratum spinosum form a large synctium. **Epithelial fibers,** described in the first part of this work, run in the exoplasm of the cells and pass from cell to cell through the cell bridges exhibiting a quite typical course (Pl. 11, Fig. 32). **Cell divisions** are always to be met with in the stratum cylindricum, where the superficial cells are replaced as they are destroyed, yet the replacement does not take place here alone, as was formerly believed, for mitoses are also found in the stratum spinosum. The cylindrical cells always contain fat in the form of minute drops about the nucleus.

2. The **stratum spinosum,** which fills the depressions between the papillæ and also covers the latter with several layers of cells. The cells are polyhedral and this stratum owes its name to the fact that the **intercellular spaces** are broadest and the **cell bridges** longest here, so that the latter look like spines when the cells are isolated. The **epithelial fibers** that pass through these cells take a rather curved course, while those in the cylindrical cells are perpendicular to the surface and are therefore parallel to the cell axes.

3. The **stratum granulosum,** which lies next to the stratum spinosum and usually consists of only a single layer of elongated cells with their longi-

tudinal axes parallel to the surface. It is composed of several layers only at the places where the horny layer is particularly thick, as on the volar surface of the fingers and toes. These cells characteristically possess numerous **coarse granules** that stain strongly with basic dyes, are soluble in acids and strong alkalies, and are digested by the gastric juice. These **keratohyaline granules** originate from the cell protoplasm in cooperation with the nucleus, and lie only in the central parts of the cell, the peripheral parts of which are free from them and contain **epithelial fibers.**

4. The **stratum lucidum,** which includes three or four layers of flat cells, and is characterized by its brilliant luster and its anisotropia. This characteristic is due to the fat that the cells contain in diffuse form, **eleidin,** a transformation product of keratohyalin, an albuminoid substance soluble in water and stained black by osmic acid. The exoplasm of these cells likewise contains **epithelial fibers,** but they lie embedded in a mass of **keratin,** which is characterized by the fact that it is only partially dissolved by strong metallic acids and by the gastric juice. It contains tyrosin. Nuclei cannot be demonstrated in the cells of this stratum.

5. The **stratum corneum,** which, as already stated, varies greatly in thickness in different parts of the body, and consists of many superimposed layers of flat, squamous, nonnucleated, **horny cells.** Each cell has a horny exoplasm containing **epithelial fibers,** and a fatty content that is probably changed eleidin. The horny exoplasms of neighboring cells blend to form the **horny lamellæ.** It is clear from what has been said that the formation of keratin is associated with that of keratohyalin, at least in the skin of the adult. It is otherwise in the fetus, where keratin is found in the cells of the periderm long before the appearance of keratohyalin.

In the colored races, and to a less degree in Caucasians, the epidermis contains a **pigment, melanin,** in the form of minute granules, found only in the cells of the stratum cylindricum and the deepest layers of the stratum spinosum, which appears for the most part after birth, even in colored people. It is secreted by the nucleus of the cells of the epidermis and is also found in the intercellular spaces.

Two layers of the **corium** may be recognized from the shape and arrangement of their connective tissue fibers. The superficial layer, the **stratum papillare,** or **papillary body,** forms the papillæ of the corium and consists of fine interwoven connective tissue fibers. The deeper layer, the **stratum reticulare,** has coarser fibers united into bundles, most of which run parallel to the surface, but often cross and interweave. The corium also contains many **elastic fibers** which are very thick and coarse in the stratum reticulare, are for the most part attached to the blood vessels, and form a very wide-meshed network. Fibers arise from this to the margin of the papillary body, where they form a second dense network of fine fibers. From this other fibers ascend to the epidermis, become very slender, and form a third network of minute fibrils just beneath the cylindrical cells (Pl. 93, Fig. 197).

Smooth muscular fibers also are present in the corium, where they run parallel to the surface in slender bundles, or unite in certain places into a muscular network. **Striated muscles** also are found entering the corium

in little bundles and passing into tendons that are lost between the bundles of connective tissue.

In addition to the flat, **fixed connective tissue cells** adjoining the bundles of connective tissue, the corium contains in many places branched **pigment cells, chromatophores,** and the so-called **lipophores,** which are also branched cells that are usually situated in the papillary body and have bodies filled with fat granules. Both they and the chromatophores may send their processes between the cells into the epithelium.

The **subcutaneous tissue** joins the skin to the subjacent parts, the muscle, fascia, or periosteum, and consists of loose connective tissue, more or less reinforced by elastic fibers that are strongest in its deepest layers. The bundles of connective tissue are either for the most part parallel, or more or less vertical to the surface of the skin, thus permitting the attached skin to be movable to a greater or less degree. An accumulation of **fat** is always formed in the subcutaneous tissue, with the exception of a very few parts of the surface of the body. The fat cells are grouped in the form of roundish or ovoid masses separated by connective tissue septa, called **retinacula.** This **panniculus adiposus** has a part to play which is by no means unimportant, both as a reservoir of fat and as an insulator to prevent loss of heat. Under certain circumstances and on certain parts of the body it may attain a thickness of several centimeters.

The Hair

The first stages of the development of the hair may be demonstrated in the skin of the face of the human embryo in the second fetal month. The cells of the germinal layer, which at this time are cuboidal, become cylindrical in circumscribed areas, place themselves with their distal ends obliquely toward one another, and bulge out the epidermal margin proximally. This **hair germ** now grows obliquely in the form of a cone into the corium and forms the **hair plug.** This consists of a superficial layer of cylindrical cells enclosing a nucleus of polyhedral ones, and forms an acute angle with the surface. On its opposite side, in the obtuse angle, it presents a distal and a proximal protrusion; the former is the rudiment of the **sebaceous follicle,** the latter the **hair swelling.** Deeply in the tissue the hair plug strikes a condensed place in the connective tissue that is rich in nuclei, which folds in about it on all sides like a hat. This is the rudiment of the **hair papilla.** The cells of the **bulb plug,** as the rudiment of the hair is now termed, adjoining the papilla, separate themselves from the rest and unite to form the **hair cone,** which rests on the papilla with a broad base, tapers distally, and passes over into a cellular cord that continues into the periderm and consists of horny cells, the so-called **hair canal.** A horny cord, a **hair,** is set free from the peripheral cells of the rudiment by the cornification of the central cells of the hair cone advancing in the cells of the hair canal, and extends from the papilla to the epidermis in a canal closed distally by the latter and running for a little way parallel to the surface. The outermost cells of the hair cone become the **inner root sheath,** while the peripheral cells of the bulb plug provide the **outer root sheath.**

The hair then gradually breaks through the layers of epidermis that cover the hair canal and juts out free. All do not break through in this manner, for there is a continuous shedding of the hair, that we shall study later.

We differentiate in the adult the ***hair*** itself, the ***root sheaths,*** and the ***hair follicle*** (Pl. 94, Fig. 201).

The part of the **hair** that projects from the skin is known as its **shaft,** that within the skin as its **root.** The latter ends in the corium, or in the subcutaneous tissue, in the **hair bulb,** a knoblike swelling that is embraced by the **hair papilla.** The hair is covered externally by a thin, transparent **cuticle,** which consists of four rows of little rectangular, quite flat, horny cells that cover it like shingles from its proximal to its distal end. The cells in the shaft and root are without nuclei, but in the vicinity of the bulb they become larger and nucleated (Pl. 95, Fig. 202).

Next, internally to the cuticle comes the **cortical substance,** consisting of nucleated, horny, spindle-shaped, elongated cells firmly joined together in many layers and forming the main part of the shaft. The cells in the bulb are denser and mixed with those of the cuticle, from which they cannot be distinguished. The cells of the cortex contain the **pigment of the hair,** which is found both in the form of intracellular granules and in solution saturating the entire cortical substance. It is brought to the cortical cells through the branched chromatophores situated in the bulb. The cortical substance also contains between its cells very minute **bubbles of air,** the multiplication of which is instrumental in causing the hair to turn gray, although the latter is also partly due to a loss of pigment, which is probably taken up and carried away by wandering cells.

The **medullary substance** forms the axis of the hair, but is developed only in its root, and is absent in hairs that are very slender. It consists of a double row of cuboidal, nucleated cells, the bodies of which contain **granules of keratohyalin.** The cellular cord broadens out like a funnel in the hair bulb and forms the inner coat of the bulb toward the papilla.

Root sheaths are developed in all hairs. Distally they blend with the layers of the epidermis, proximally they first become thin and then form a cellular mass covering the base of the bulb and surrounding the papilla. They are divided into an ***inner*** and an ***outer.*** The former is simply a continuation of the germinal layer of the epidermis; the latter begins a little way from the surface, adjoining the stratum granulosum of the epidermis, which extends as far as this.

There is little to be said of the **outer root sheath;** it resembles exactly the germinal layer of the epidermis, and like it has epithelial fibers. Proximally it grows thinner gradually and is lost in the hair bulb.

The structure of the **inner root sheath** is more complicated. It has three layers. Next to the outer root sheath lies **Henle's layer,** a single or double row of cells that are joined by their epithelial fibers with those of the outer root sheath. Beginning distally, at the end of the stratum granulosum, its cells are flat, elongated, without nuclei, and **horny;** proximally they become denser, nuclei appear, cornification disappears, and **granules of keratohyalin** are to be seen in them. Internal to this is **Huxley's**

layer, composed of two layers of polyhedral cells. These also are ***cornified*** distally, but the horny cells cease earlier, and those containing nuclei and keratohyalin begin sooner than in Henle's layer (Pl. 95, Fig. 202). The root sheaths are bounded internally by the **cuticula,** formed of horny scales that change proximally into nucleated cells. The cuticula of the root sheaths thus directly adjoins that of the hair. In the bulb the cells of the inner root sheaths form the main part of those lying peripherally and proximally from the cells of the cortical substance. The separate layers can be perceived at first, but later they all unite into a uniform mass of cells.

The **hair follicle** is found only with the larger hairs, and consists of an outer layer of **bundles of connective tissue** running longitudinally and reinforced by elastic fibers, next to which is a second layer in which the bundles of connective tissue have a circular course. It is bounded toward the outer root sheath by the homogeneous **vitreous membrane,** in the formation of which the connective tissue of the follicle and the cells of the outer root sheath take equal parts.

A **shedding of the hair** takes place continually in man; old hairs are cast off and replaced by new ones. The casting off of the old hair is introduced by a process of cornification that starts in the bulb. The shaft of the hair is thereby detached, swells at its end like a club, and breaks up into fibers. Proximally the hair root, now become solid through the proliferation and cornification of its root sheaths, draws out into a slender cord with the reduced bulb and the flat papilla hanging on its end. The formation of a new hair now proceeds from the hair swelling already described, which appertains to the outer root sheath, and practically follows the embryonal type. The old hair is thrust out gradually by the pressure of the one newly formed.

Human hair is provided with a special **musculature,** the **arrectores pilorum** (Pl. 94, Fig. 201). The cilia, eyebrows, vibrissæ of the auricle, and the beard are rigid, immovable hairs not provided with these muscles. The arrector pili is a roundish bundle of **smooth muscle fibers** that passes obliquely through the obtuse angle formed by the hair and the surface. It arises from the stratum papillare, runs backward obliquely to the hair bulb, and is inserted into its longitudinal outer layer by means of a short tendon reinforced by elastic fibers. Its contraction, which is produced by psychic or thermic stimuli, erects the hair and presses it somewhat out from the skin, producing what is known as goose-skin.

The Nails

The development of the nail begins in the third month on the extensor surface of the terminal phalanx, the **nail field,** a place of thickened epidermis that becomes more and more distinct from its neighborhood, which gradually comes to resemble a wall. This wall turns in at the margin of the nail field, forming the **nail fold.** The **substance of the nail** begins to be produced in the fifth month through cornification of the middle layers of epidermis without any preliminary formation of keratohyalin. Thus the nail is covered by the peripheral layers of epidermis, the **eponychium.** The deeper layers of the epidermis arrange themselves on the under surface of the nail into longi-

tudinally running ridges which are closer behind than in front. The ridges of the corium that correspond to those of the epidermis have no papillæ in the greater part of the bed of the nail. The nail is therefore at first invested by epidermis, through which it breaks toward the end of embryonal life.

The nail consists of the ***stratum corneum*** and the ***stratum germinativum.*** The former consists of horny, scalelike cells united together into several superimposed plates arranged like shingles. Bubbles of air often form between the plates and, when large, create whitish spots. The stratum corneum ceases in the nail fold with laterally sharpened margins, its outer surface covered at this place by the corneal layer of the nail wall that continues for a way over the free surface as the eponychium.

The **stratum germinativum** is a direct continuation of the germinal layer of the nail wall, in front of which it is characterized by a regular formation of ridges that are considerably narrower in the back part, which is delimited from the front by a convex line. So far as this back part extends free from the nail fold it forms the **lunula** of the nail. In front, at the place where the nail plate separates from the finger tip, the germinal layer of the nail is continuous with that of the pulp of the finger. The latter naturally also has a stratum corneum, called the **hyponychium,** which covers the under surface of the free nail plate, and therefore consists of the hyponychium and a stratum corneum.

The **nail bed** is the corium, and has on its surface a system of ridges corresponding to those of the stratum germinativum. Papillæ are present only in the back part of the root of the nail. The ridges consist of longitudinally running bundles of connective tissue with vertical ones in the stratum reticulare (Pl. 96, Fig. 204).

The Sweat Glands

The **sweat glands** originate as solid protrusions, partly of the free ridges of epidermis, partly of the most distal parts of the hair rudiments, beginning in the fourth month, and appear first on the volar surfaces of the fingers and toes. The cellular plugs that look exactly like hair rudiments grow deeply into the tissue and gradually become canalized in various places. The young glandular tube then has a double layer of cuboidal epithelium. The canal coils up at its proximal end as it continues to grow and forms the body of the gland, within which the two layers of cuboidal cells are transformed into long contractile cells.

An **excretory duct** and a **body** may be differentiated in each sweat gland. The **excretory duct** starts from the **sweat pore** at the surface of the skin, passes through all the layers of the epidermis in corkscrewlike spirals, and enters the corium between two of its papillæ (Pl. 93, Fig. 198). In this first part of its course the canal has no wall of its own, but simply winds between the cells of the stratum corneum, but in the deeper layers of the stratum spinosum a cellular wall gradually develops, composed of two layers of cuboidal cells, the inner of which is particularly marked by its homogeneous, strongly staining protoplasm. Within the corium the canal usually runs rather obliquely to the surface and has here an outer layer of high cuboidal

cells and an inner one of much lower cuboidal cells. Externally it is surrounded by a structureless membrana propria.

The **body of the sweat gland** lies either in the deeper layers of the corium, or in the subcutaneous tissue, and has an average diameter of from 0.1 to 0.4 mm. In it the duct forms several coils and ends with a rounded top. The lumen of the excretory duct becomes not inconsiderably wider at its entrance into the body and the entire tube becomes thickened externally. The inner, low cuboidal cells disappear, leaving the tube lined with high cuboidal or conical ones, that are a continuation of the outer layer of cells of the excretory duct. The cells are provided with a thin cuticular border on the free surface, while between them **secretory capillaries** penetrate from the lumen and give off lateral branches that pass into the epithelial cells themselves. Each cell contains a spherical or ovoid nucleus situated about in its center, and a rodlike central body. The cell body contains mitochondria in its basal part, particles of fat, granules of pigment and secretion in its distal (Pl. 94, Fig. 200).

Externally lies a layer of flat, long, secretory cells, which ramify a great deal, anastomose, and must be considered from their entire configuration as **contractile elements.** Outside of this the glandular canal is bounded by the structureless **membrana propria.**

The **sweat,** or **perspiration,** the secretion of the sweat glands, is a clear, acid fluid that contains on an average 1.5% of solid constituents, including albumin, urea, creatinin, aromatic oxacids, neutral fats and fatty acids. It is very poisonous when injected into the veins.

Among the **modified sweat glands** are the **Moll's glands** of the eyelids, and the **ceruminous glands** of the external auditory meatus. The **axillary glands** also should be included, as they differ from the ordinary ones in their unusual size and the branching of their excretory ducts.

The Sebaceous Glands

Most **sebaceous glands** develop as diverticula of the most distal parts of the hair plugs and remain throughout life connected with the hair follicles. They occur alone in only a few parts of the body, such as the red portion of the lips and the labia minora. They are **branched alveolar glands,** and each opens with a short neck into the distal end of the hair follicle. The short excretory duct soon divides into several branches that are studded with many spherical **alveoli** (Pl. 94, Fig. 201). The **epithelium** of the excretory duct is the direct continuation of the outer root sheath of the hair follicle, and like it is **stratified.** It passes over into a mass of large polyhedral cells filling the alveoli, in each of which an exquisitely vacuolized protoplasm encloses a frequently deformed nucleus. Drops of fat lie in the vacuoles. The fatty degeneration of the cells proceeds from without inward, and a **destruction of them** takes place in the centers of the alveoli. The most peripheral layer of cells contains no fat, their nuclei are round and are very often in a condition of mitosis; they serve to replace the cells destroyed during secretion. The cell body contains numerous mitochondria, from which the drops of fat originate in the central layers through metamorphosis.

The arrector pili, which passes along the outer side of the gland, plays an important part in the expulsion of the secretion, the **sebaceous matter,** which is semifluid and contains albumin with a fatty body.

The Blood Vessels of the Skin

The **arteries of the skin** form two extensive superficial plexuses, the deeper of which is situated between the subcutaneous tissue and the corium, the more superficial beneath the bodies of the papillæ. The two anastomose freely and the deeper is fed by main trunks rising out of the deeper tissues. The branches springing out of the superficial plexus run at first horizontally beneath the rows of papillæ, sending a twig into each, and terminate in the same way themselves. The arteries break up into loops of capillaries in the papillæ (Pl. 93, Fig. 198). The efferent **veins** form several plexuses, two of which are subpapillary, and two are situated in the deeper layers of the corium. The **arteries of the hair** branch from the arterial plexus of the corium and form a capillary plexus in the inner longitudinal layer of the hair follicle and an arborization in the papilla (Pl. 95, Fig. 202). About the body of each sweat gland is an arterial plexus from which twigs enter the body itself and form capillary plexuses about all the coils of the glandular tube.

The Lymphatics of the Skin

We find enclosed lymphatics lined with epithelium everywhere in the skin. They form networks in the corium that penetrate into papillæ, but always lie beneath the vascular plexuses. It is uncertain as yet whether the hair follicles contain lymphatics or not.

The Nerves of the Skin

The nerves of the skin are very numerous and consist for the most part of medullated fibers with a smaller number of nonmedullated. They form several plexuses, the deepest of which is in the subcutaneous tissue, the most superficial just beneath the papillæ. Part of the fibers coming from these plexuses terminate free in the epithelium, part in special end formations, part on the cutaneous glands (Pl. 97, Figs. 205 and 206).

The **fibers that enter the epidermis** lose their medullary sheaths before their entrance and break up into more or less fine fibrils that rise between the cells of the epidermis and give off lateral twigs which either run out into fine points, or end in little thickenings. Under certain circumstances the branches may anastomose so as to form an intraepithelial plexus. **Merkel's tactile discs** are special end formations of the intraepidermal nerve fibers that are but sparingly present in man. They occur only in the deepest layers of the epidermis, especially in the vicinity of the ducts of the sweat glands, and are cup- or dish-shaped, with the concavity directed distally. A twig from a nerve fiber ends in the wall of the dish in the form of a plexus provided with marked expansions. In the cup lies a spherical cell, which is nothing else than a somewhat modified epidermal cell. Several such tactile discs are attached to each nerve fiber, which sends a twig to each disc.

Free nerve endings are also met with in the **connective tissue portion** of the skin in the form of treelike branchings, the ends of which not rarely terminate in end plates. They occur most of all in the bed of the nail, but are met with elsewhere. On the **hairs** the fibers, having lost their medullary sheaths, form first a circular plexus situated within the connective tissue hair follicle, from which other fibers form another plexus internally on the vitreous membrane with elongated meshes, from which numerous very minute longitudinal fibrils rise and end free. In the hair papilla we meet only sparingly with nerve fibers going to the musculature of the vessels.

The **encapsulated nerve endings** are very much more manifold than the free, and we can describe here only a few of the most important.

The **Vater-Pacini corpuscles** have a maximum size of 4 x 2 mm, are ovoid in shape, and are distributed very widely, especially in the subcutaneous tissue of the flexor surface of the hands and feet, fingers and toes, but are also found in the periosteum and in other places (Pl. 93, Fig. 197; Pl. 96, Fig. 204). The axis of the corpuscle is formed by a nerve fiber which loses its medullary sheath at its entrance, and swells like a club at its end. The axis cylinder is surrounded by a **dense protoplasmic sheath** with flat cells adjoining it internally, enclosed in an extremely fine, close-meshed nervous plexus that originates from a second nerve fiber which enters together with the first, but differs from it in being extremely slender, and then surrounded by a large number of connective tissue **concentric sheaths** that lie at first very close together, then farther apart toward the outer surface, all so filled with a serous fluid that the entire corpuscle seems to be tense. The inner side of each lamella is lined with epithelial flat cells.

Krause's end bulbs, found especially in the bulbar conjunctiva, are a simpler variety of the Vater-Pacini corpuscles. They likewise consist of an axis cylinder surrounded by a dense protoplasmic sheath, but this is enclosed in only a single connective tissue sheath, so the formations are more slender and cylindrical.

The **Golgi-Mazzoni corpuscles** are found in the bed of the nail, but mainly on the skin of the external genitals. They are usually similar in shape to the Vater-Pacini, but are considerably smaller. The envelope is similar, but is commonly composed of only a few lamellæ. The interior of the corpuscle is filled with a mass of protoplasm. The entering nerve fiber divides, after losing its medullary sheath, into numerous ramifying branches that are studded with irregular thickenings and expansions in which they also terminate. The thick principal fiber is often accompanied by a thinner one that forms a fine plexus on the inner surface of the capsule.

Meissner's corpuscles enjoy a wide distribution in man. They lie in the papillæ of the corium just beneath the epidermis, are most numerous in the skin of the flexor surface of the fingers and toes, are oval, and have a maximum length of 150 μ, with a breadth of 100 μ. Each is enclosed in a thin connective tissue capsule that penetrates into the corpuscle and divides it into two to four **lobes.** One or more medullated fibers enter the corpuscle, lose their medullary sheaths, divide, and form in it loops usually placed vertically or obliquely to the longitudinal axis, and studded with varicosities.

Between the loop lie cells, some of which are to be considered tactile, some to be connective tissue cells. A slender nerve fiber enters Meissner's corpuscle, together with the thick one, and weaves a terminal plexus about the loops.

Many other forms of tactile corpuscles are met with in animals, and especially in birds, some of which are simpler, some more complicated (Pl. 97, Figs. 205 and 206).

The Mammary Gland

The mammary is a **cutaneous gland** and starts as a diverticulum of the epidermis. Its rudiment may be seen in embryos of the fourth fetal week in the form of the so-called **milk stripe,** a thickening of the epithelium that forms a longitudinal stripe on each side of the body between the rudiments of the upper and lower extremities. The **milk ridge** is formed from this in the second fetal month by its becoming more thickened and projecting inward. This soon breaks up into separate successive rudiments, of which only one survives on each side in man, to undergo further development. It grows like a bulb into the corium and sends out shoots during the second half of fetal life that are at first solid, but later become hollow. Toward the end of pregnancy the bulb itself becomes hollow, dilates, flattens, and then raises a **nipple,** where the **milk ducts** open singly. The latter are provided with vesicular protrusions at their proximal ends. The mammary gland is thus developed uniformly in both sexes at the time of birth. It undergoes involution during youth in boys, but develops further in girls through the formation of new milk ducts. At the time of puberty the entire female breast becomes larger and more prominent through a great development of fat. During pregnancy a further marked development of the glandular tissue takes place, in which the milk ducts divide repeatedly at their ends and end pieces are formed.

The **functionating mammary gland** of the nursing woman is therefore a conglomerate of seventeen to twenty **compound branched alveotubular glands,** each of which has its own **milk duct** that opens at the nipple. Each separate gland forms a **lobe** of the entire organ, which is embedded in a fatty connective tissue that penetrates into the lobes and divides them into many **lobules.** These lobules contain the end pieces (Pl. 98, Fig. 207). After **lactation** has continued seven or eight months a great part of the end pieces undergo involution, and the loss is made up by newly formed more or less fatty connective tissue.

The secretion of the mammary gland is **milk,** a neutral fluid that has the character of an **emulsion.** The **milk plasma** contains dissolved sugar and albumin, together with inorganic salts. The sugar is **lactose,** the albumin is chiefly **casein,** which is not coagulated by heat. In this milk plasma are suspended **milk globules,** drops of fat of variable size consisting mainly of **neutral fat.** Milk also contains very minute granules, probably of calcium phosphate. The **colostrum** secreted at the beginning of lactation differs from milk in its yellow color, due to the presence of **colostrum corpuscles,** and the greater amount it contains of **lactalbumin** and of **lactoglobulin,**

which cause it to be coagulable by heat. The colostrum corpuscles are migrated leucocytes, the bodies of which are full of fat granules.

The **milk ducts** are first lined with **stratified flat epithelium** that rests on a structureless **membrana propria.** Just before it opens in the nipple it dilates into a **milk saccule,** in which the epithelium becomes simple cylindrical. The **excretory duct** leading out of the milk saccule has the same structure and soon divides into the **interlobular ducts,** which divide again into the **intralobular ducts.** All of these have the same structure—a lining of **simple cylindrical epithelium** covered externally by a membrana propria. Between the two are flat nuclei which belong to branched **contractile basket cells** that surround the canal. The intralobular ducts pass into the **alveolar end pieces,** which have the same structure. The appearance of the epithelium varies according to the stage of the secretion. **Cells filled with secretion** are high cylindrical or conical and project their tops into the lumen. The distal part of the cell contains a granular, clear protoplasm that holds numerous larger and smaller drops of fat. The proximal part contains one nucleus, often two, surrounded by a darker protoplasm that holds many tortuous, filamentous mitochondria (Pl. 98, Fig. 208).

The **expulsion of the secretion** from the cell is pictured differently by various authors. Some think that the drops of fat and the secretory granules simply leave the uninjured cell, while others believe that the entire distal part of the cell, with one of the two nuclei, is thrown off into the lumen, so that a sort of decapitation of the cell takes place. The nuclei that are destroyed are replaced by amitosis of those that remain. However this may be, the **empty cells** are low cuboidal, have a nucleus and mitochondria, through the breaking down of which and the metamorphosis of its constituents the secretion is produced.

External to the secretory are the **basket cells,** and outside of these is the **membrana propria.**

The **arteries** of the mammary gland come from the internal mammary and the intercostals. They branch in the interlobular and intralobular tissue, enter the lobules, and form capillary plexuses about the end pieces. The **veins** follow generally the course of the arteries.

The **lymphatics** surround the end pieces and form plexuses about the milk ducts. They are connected with a plexus in the corium of the skin. The efferent vessels run to the pectoral, paramammary, sternal, interpectoral, and interclavicular lymphatic glands.

The **nerves** come from the intercostals and from branches of the brachial and cervical plexuses. Very many of their fibers are nonmedullated, together with others that are medullated. They form first a perialveolar plexus within the lobule, from which fibers pass through the membrana propria and form the plexus intercellularis about the bases of the secretory cells, that send very minute fibrils between the cells, where they terminate in little end nodules.

The **skin of the areola of the nipple** differs from that about it in its thinness, in its pigmentation, and in its plenitude of elastic fibers. It also possesses in its papillary bodies a well-developed system of **smooth muscle**

fibers, part of which surround the milk ducts, part are radiating, and part run vertically to the surface. Together they form what is known as the **areolar muscle,** which extends into the nipple and produces by its contraction an erection and a marked protrusion of the latter. The corium in the areola of the nipple is peculiarly rich in *glands.* We find here many **sweat glands,** that are distinguished by their size, and well-developed **sebaceous glands,** each with a rudimentary hair follicle, that enlarge considerably during pregnancy and lactation. Finally, we find here the **accessory milk glands,** or **Montgomery's glands,** which, to the number of twelve or fifteen, lie in the subcutaneous tissue and are nothing else than miniature mammary glands, each corresponding to a single lobe of the larger organ.

The skin of the areola of the nipple and of the nipple itself is very richly supplied with **sensory nerves,** part of which terminate free in the epidermis, part in special end formations. Among the latter we find Meissner's corpuscles within the papillæ of the corium, which are very high, and the Vater-Pacini corpuscles in the deeper layers of the corium.

THE COPYRIGHTS OF THIS BOOK, IN ALL ENGLISH-SPEAKING COUNTRIES,
ARE OWNED BY REBMAN COMPANY, NEW YORK.

INDEX

Accommodation, 223, 227
Accretion lines, 38
Achromatic framework, 6
  membrane, 6
  substance, 6
Acramines, 217
  diffuse, 217
  stratifying, 217
Adenoid tissue, 82
Adrenalin, 150
Afterbrain, 197
  nuclei, 197
  olive, 198
  pyramids, 197
Aggregated follicle, 80
Albuginea, 153, 163
  definitive, 165
  primary, 165
Alveolar passages, 127
  septa, 128
Alveoli, 127
Amitosis, 11
Amœboid movement, 5
Amphicytes, 195
Amphipyrenin, 6
Amylopsin, 117
Anaphase, 12, 14
Annulus fibrosus, 77, 184
  tendineus, 247
Appendix, 108
Appositional growth, 60, 181
Aqueous, 224
Arachnoid, 210
Arachnoidal space, 210
  villi, 210
Archispermatocytes, 154
Archoplasm, 7, 13
Areola, inner cell, 59
  outer cell, 59
Arrectores pilorum, 257
Arteriolæ rectæ spuriæ, 143
  veræ, 143
Arterioventricular bundle, 77
  valves, 78
Artery, coronary, 78
  penicillate, 83
  precapillary, 73
  thecal, 83
Astrocytes, 47, 218
Atresia of follicles, 169
Auditory basilar fibers, 242
  canal, 248
  cup, 238
  hairs, 240, 243
  meatus, 247
  nerve, 198, 210
  ossicles, 245
  plate, 247
Auditory teeth of *Huschke*, 242
  vesicle, 238
Auerbach's plexus, 110
Aural folds, 247
  eminences, 247
Axis cylinder, 43, 45
  filaments, 160
Axoplasm, 46

Baillarger's stripes, 208
Bartholin's glands, 176
Basal filament, 97
  homogeneous, 242
  membrane, 107, 125, 130
  substance, 89
Basic substance, 57, 59
  cartilage capsule, 59
Basophilic chromatin, 5
Bechterew's nucleus, 199
Bile, 114
Biliary capillary, 114
  pigments, 113
  salts, 113
Bilirubin, 113
Biliverdin, 113
Bladder, 145
  adventitia, 146
  arteries, 146
  crypts, 146
  epithelium, 145
  glands, 146
  lymph follicles, 146
  lymphatics, 146
  membrane, 146
  mucus, 146
  muscularis, 146
  nerve fibers, 146
  propria, 146
  submucosa, 146
  veins, 146
Blandin-Nuhn glands, 93
Blind spot, 219
Blood, 66
  corpuscles, 66
    primitive, 66
    red, 66, 67, 82
    white, 67, 68
  corpuscular elements, 71
  functional, 114
  islands, 66
  nerves, 76
  plasma, 66
  platelets, 70
  primitive, 72
  secondary, 73
  shoots, 72
  vessels, 72, 76
Bone, 181
  arteries, 182
  basic substance, 62, 64
  canaliculi, 64
  cavities, 64, 89
Bone cells, 64, 89
  compact, 63, 181
  corpuscles, 65
  lamellar structure, 63
  lymphatics, 183
  marrow, 181
  nerves, 183
  physical properties, 63
  primary, 61
  regeneration, 181
  secondary, 61
  substance, compact, 62
    spongy, 62
Bowman's capsule, 138, 140
  glands, 250
  membranes, 228
Brain, 39, 197
  sand, 207
Bronchi, 125
  extrapulmonary, 125
  intrapulmonary, 126
  lateral, 127
  main, 127
Bronchioles, 127
  intralobular, 127
  respiratory, 127
Brown's molecular movement, 196
Bruch's membrane, 225
Brunner's glands, 109
Bundles of *His*, 39
Burdach's column, 188, 191, 192
  nucleus, 192

Cajal's cells, 207
Calcareous epithelium, 18
Calcification points, 62
Calices majores, 137
  minores, 137
Canalis reuniens, 239
Capillary, 73
  basket, 104
  intracellular, 31
  secretory, 31, 97
Carcinoma, 4
Cardiac muscle fiber, 38
Cardiogenous plate, 76
  plexus, 79
Carotid gland, 151
Cartilage, 58, 60
  capsule, 59
  cavity, 58
  cell, 58
  elastic, 58, 61
  fibro, 58
  hyaline, 58
  reticular, 68, 61
Caruncula lacrimalis, 235
Casein, 262
Caudal section, 171

Cavity of vitreous, 214
primary medullary, 62
Cell, 1
basket, 97
biological properties, 7
bipolar, 41
body, 2, 14, 59
bridge, 19, 21
budding, 15
cartilage, 58
chief, 131
chordal, 50
chromaffin, 149
colloid, 131
constriction, 15
construction, 2
cover, 22
crenated, 22
cuboidal, 242
cylindrical, 5, 172, 242
ependymal, 47
fat, 53
filiform, 24
foot, 154
form, 1
giant, 4
goblet, 18, 108
hair, 24
manifestation of life in, 8
mast, 52, 54
membrane formation, 2
metabolism, 8
motor, 41
multipolar, 41
muscular, 32
nucleus, 2, 4
oxyphilic, 133
peg, 108
pigment, 10, 53
plasma, 52, 54
plates, 14
polynucleated, 4, 15
prickle, 22
primitive spermatic, 154
propagation of, 11
pyramidal, 189
reaction of, to external stimuli, 10
reticular apparatus, 2
rod, 83
segmentation, 8, 15
indirect, 12
sensory, 41
size, 1
smooth muscle, 73
spermatic mother, 154
stellate, 188
striated muscle, 33
territories, 59
umbrella, 22
unipolar, 41
wandering, 52, 53
water in, 9
Cement, 19, 63, 87, 88, 89
edges, 19, 20
lines, 64
striæ, 38
Central bodies, 2, 6, 44, 54
canal, 193
corpuscles, 33
Central formation, 2
spindle fibers, 13
Centrodesmose, 6
Centrophornium, 229
Centrosome, 7
Centrosphere, 7
Cerebellum, 201
arteries, 203
cells, 201
cortex, 201
fibers, 202
neuroglia, 202
nuclei, 203
Cerebral cortex, 190
Cerebrospinal fluid, 210
Cerumen, 248
Choledochus, 116
Chondral stage, 58
Chondrin, 60
Chondriosomes, 2, 7, 12
Chondroblast, 57
Chondroid connective tissue, 61
Chondroitin-sulphuric acid, 57, 60
Chorda dorsalis, 50
Chordal epithelium, 50
sheath, 50
Choroid, 221
blood vessels, 221
lamina, 221
Chromatic membrane, 5
substance, 6
Chromatin, 5, 8
oxyphilic, 5
Chromatophores, 255
Cilia, 234
Ciliary body, 222
muscle, 222
processes, 222
vascular system, 231
Circulus arteriosus iridis major, 232
Cisterna perilymphatica, 245
Clarke's cells, 189, 191
Clasmocytes, 52, 54
Climacterium, 173
Clitoris, 176
glans, 176
prepuce, 176
Cochlear process, 239
Cohnheim's fields, 35
Collaterals, 42
Collecting tubules, 137, 139
Collegen, 55
Colloid, 131
Colostrum, 262
corpuscles, 262
Column of *Burdach*, 186, 191
Clarke, 189
Goll, 186, 191
Commissure, gray, 186, 190
white, 186
Cone, 216
bipolar, 217
ellipsoid, 216
fiber, 217
foot, 217
granule, 216
myoid, 216
optic cell, 217
Conjunctiva, 233
arteries, 235
bulbi, 234
cavity, 234
lymphatics, 236
nerves, 236
palpebrarum, 234
veins, 235
Contraction nodes, 33
Convoluted tubule, 138, 140
Corium, 248, 252
Cornea, 227
anterior chamber, 227
cells, 227
connective tissue, 228
epithelium, 227
fibers, 228
lymph canals, 228
Corneal corpuscles, 228
Cornification, 252
Corona radiata, 168, 205
Corpus albicans, 169
cavernosum, 162, 176
dentatum, 203
geniculatum, 204
luteum, 169
quadrigeminum, 204
Corpuscular elements, 79
Cortex, cerebral, 207
arteries, 208
cells, 207
fibers, 208
neuroglia, 208
Cortical substance, 134
Corti's membrane, 244
organ, 241, 242, 243
tunnel, 242
Cowper's glands, 159
Crusta, 4
Cumulus ovigerus, 167
Cupola terminalis, 240
Cuticula, 87
dentis, 88, 89
Cutis, 252
Cylindo-conical segments, 47
Cytomitome, 3

Daughter stars, 14
Decussation of the pyramids, 197
Deiter's cell, 243
nucleus, 199
type, 42
Dental canaliculi, 88
groove, 86
papilla, 86
pulp, 90
blood vessels, 90
lymphatics, 90
nerves, 90
root, 87
tubules, 88
Dentine, 65, 87, 88
basal substance, 88
fiber, 90
globules, 88
interglobular spaces, 88
Dentrites, 39
Descemet's membrane, 228
Deutoplasm, 3, 4

Diaphragm, 130
arteries, 130
innervation, 130
lymphatics, 130
muscular part, 130
tendinous part, 130
veins, 130
Digestive organs, 84
Dilator iridis, 224
Dimples, primitive gastric, 101
Dioptric apparatus, 214, 227
Diploe, 181
Directing bodies, 168
Discs, 35
Distal layer, 214
Drum, 245
Ductus cysticus, 116
endolymphaticus, 238, 245
epididymitis, 156
perilymphaticus, 245
Dura mater, 210

Ear, external, 247
arteries, 248
cartilage, 248
connective tissue, 247
epidermis, 247
epithelium, 247
glands, 248
hairs, 248
lymphatics, 248
membrane, 247
mucosa, 247
nerves, 248
propria, 247
veins, 248
Ear, internal, 238
ampulla, 238
arteries, 244
blood capillaries, 241
cells, 244
crista spiralis, 241
ganglion, 238
membranes, 240
nerves, 240, 244
pars dorsalis, 238
perilymphatic spaces, 245
plate, 238
prominentia spiralis, 241
spiral ganglia, 244
veinous blood, 244
ventralis, 238
vertical pouch, 238
vestibular wall, 241
Ear, middle, 245
arteries, 246
cartilage, 246
epithelium, 245
fibers, 246
glands, 246
lymph follicles, 246
lymphocytes, 246
membrane, 245
muscles, 246
nerves, 246
ossicles, 246
propria, 245
veins, 246
Ebner's glands, 93
Ectoderm, 149, 214, 224, 256
Ectoplasm, 4
Elastic cartilage, 58
network, 130
Elastica externa, 75
interna, 74, 75
Elastin, 55
Electrical force, 11
Eleidin, 254
Embolus, 203
Enamel, 18, 87, 89
cells, 87
cuticle, 89
membrane, 87
organ, 86
prism, 88, 89
pulp, 87
Endocardium, 77, 78
Endolymph, 245
Endometrium, 172
Endoneural sheath, 213
Endoneurium, 213
Endothelium, 20
Enterokinase, 111
Entodermal cloaca, 145
Enzymes, 4
Epidermis, 22, 252
Epididymis, 156
Epineurium, 212
Epiphysis, 206
Epithelial cells, 19
fibers, 22
Epithelium, 20, 76
cardiac, 77
enamel, 87
epicardial, 78
flat, 129
glandular, 24
respiratory, 128
sensory, 24
simple cuboidal, 20
cylindrical, 21
flat, 20
stratified, 21
cylindrical, 22
flat, 21
stratiform, 23
ciliated, 23
transitional, 22
vascular, 73
Eponychium, 257
Epoophoron, 166
Equatorial plate, 13
Erepsin, 111
Erythroblasts, 182
Erythrocytes, 66, 67
Eustachian tube, 246
Exoskeleton, 61
osseous, 61
External female genital organs, 176
Eye, 214
cells, 218
fibers, 218
ganglion, 218
muscles, 214
Eyeball, 231
blood vessels, 231
lymphatics, 232
nerves, 233
Eyelids, 233

Fallopian tube, 170
arteries, 171
cilia, 171
epithelium, 170
folds, 170
lymphatics, 171
membrane, 170
muscularis, 171
nerves, 171
propria, 171
secretion granules, 171
submucosa, 171
veins, 171
Fascia palpebralis, 199
penis, 163
Fasciculus longitudinalis medialis, 199
Fat, 3, 59
Fatty capsule, 57
Female genital organs, 165
Fenestrated membranes, 55
Ferment profibrin, 71
Ferments, 103, 111
Fiber, branched muscle, 34
cardiac muscle, 77
collagenous, 54, 73
connective tissue, 54
elastic, 54, 61, 73, 125
firm, 47
medullated sensory, 76
muscular, 130
nonmedullated, 76
radiating elastic, 74
smooth muscle, 74, 166
striated muscle, 34
supporting, 47
tendinous, 130
Fibræ arcuatæ internæ, 198, 203
Fibrillary network, 51
Fibrils, 3, 38, 51
collagenous, 59, 63
contractile, 32, 34
internal, 33
limiting, 33
transversely striated, 38
Fibroblast, 52
Fibrocartilage, 58, 60
Fibrocartilagines intervertebrales, 184
Fibroelastica, 181
Fimbriæ, 170
Fissura longitudinalis anterior, 186
Flagella, 11
Flechsig's bundles, 189
Follicle, 30
cortical, 81
lingual, 92
lymph, 92
primary, 165
solitary, 80
Follicular cells, 167
epithelium, 166
Fontana's space, 229
Foramina nervina, 244
Foreskin, 163
Fornix, 236
Fovea centralis, 215, 219
Framework, 59

Frenulum, 162
clitoridis, 176
Frog, 5
Fuscin, 216

Gall bladder, 115
epithelium, 116
membrane, 116
muscularis, 116
nerves, 116
propria, 116
Ganglia, 39
cerebral, 211
Ganglionic crest, 195
Gastric dimples, 102
glands, 103
mucus, 102
Gelatin, 55
Gelatinous nucleus of intervertebral discs, 50
Genital cord, 165, 170
eminence, 162, 176
folds, 162, 176
prominences, 162, 176
Germinal center, 80
epithelium, 166
spot, 167
vesicle, 5, 167
Gianuzzi's crescents, 97
Gland, 24
acinous, 28
alveolar, 25, 27, 28
alveotubular, 25, 28, 29
base, 26
body, 25
branched, 25
cardiac, 104
cervical, 173
ciliary, 234
closed, 25, 29
compound, 25
convoluted, 25
fundus, 103
gastric, 102
hæmolopoietic, 25
labial, 85
lacrimal, 235
lingual, 92, 93
neck, 25
ovarian, 166
palatine, 94
parotid, 95
pyloric, 103
serous, 93
simple, 25
solid, 25, 29, 30
sublingual, 95
submaxillary, 95
true, 25
tubular, 25, 26
uterine, 172
vestibular, 176
Glandular cavity, 24
cells, 24
Glia cell, 47
fiber, 41, 47, 48
tissue, 41, 47
Glisson's capsule, 113
Glomerulus, 140, 142
olfactorius, 209
Glomus coccygeum, 151
Glue, 55
Glycogen, 3, 36, 59, 113, 114
Golgi-Mazzoni corpuscles, 261
Golgi's type cells, 42
secondary, 189, 208
Goll's nucleus, 191
Gower's tract, 191
Graafian follicles, 167
Granules, 30, 54
Granulosa, 179
Gray matter, 188
columnar cells, 188
commissural cells, 188
nerve cells, 188
nerve fibers, 188
root cells, 188
Ground plate, 223
Gums, 88, 90

Hæmoglobin, 66
crystals, 67
Hæmokonia, 71
Hæmotoxylin, 5
Hair, 255
canal, 255
cells, 256
cone, 255
connective tissue, 257
cortical substance, 256
cuticle, 256
fiber, 257
follicle, 255
germ, 255
medullary substance, 256
musculature, 257
papilla, 255
pigment, 256
plug, 255
root sheath, 255
shedding, 257
swelling, 255
vitreous membrane, 257
Haller's circular arterial plexus, 231
Hassel's corpuscles, 134
Haustra, 109
Haversian canals, 62, 64, 89
lamellæ, 64
Heart, 76
ganglia, 79
muscle fiber, 77
nerves, 78
skeleton, 77
valves, 78
vesicular supporting tissue, 77
Heat, 11
Heidenhain's rods, 96
Helicotrema, 240
Helweg's tract, 191, 198
Henle's fibrous layer, 217
layer, 256
loop, 137, 139
Hensen's body, 243
canal, 240
Hepatic duct, 113
lobules, 113
Highmore's corpus, 153
Hilus of the gland, 81
Hippuric acid, 138
His' bundle, 77
Hollow spaces, 167
Huxley's layer, 256
Hyaline cartilage, 58
Hyaloid canal, 230
Hyatoplasm, 3
Hydatids, pedunculated, 170
Hydrochloric acid, 103
Hymen, 175
Hyponychium, 258
Hypophysis, 205
arteries, 206
cells, 206
nerves, 206
veins, 206

Idiosome, 154
Infundibulum, 127
Interbrain, 203
floor, 205
Intercalares fibrocartilagines, 60
Intercellular bridges, 19
clefts, 19, 20
spaces, 19, 21
substance, 19, 49, 54
Interlobular ducts, 113
Intermediate disc, 47, 184
Interpolated sections, 38
Interstitial granules, 38
growth, 60
substance, 36
Intervening tendons, 38
Intestinal juice, 111
Intestine, 105
arteries, 109
epithelium, 106
folds, 106
lymphatics, 110
membrane, 106
muscularis, 109
nerves, 110
propria, 106
submucosa, 106, 109
Invertine, 111
Involucrum, 161
Iodine, 131
Iris, 222, 224
epithelium, 225
nerves, 233
pigment, 225
stroma, 224
Irregular leaves, 38

Jacobson's organ, 249
Joints, 183
articular capsules, 183
surfaces, 183
blood vessels, 184
intima, 183
lymphatics, 184
nerves, 184

Keratin, 18, 254
Keratohyaline granules, 252, 256
Kerkring's folds, 106
valves, 106

Kidney, 136
arteries, 142
cortex, 141
definitive, 136
lymphatics, 143
medulla, 141
nerves, 143
pelvis, 137, 144
stroma, 142
veinous blood, 143
veins, 143
Kidney pelvis, 144
adventitia, 144
arteries, 144
lymphatics, 145
membrane, 144
nerves, 145
propria, 144
transitional epithelium, 144
Kinase, 71
Krause's corpuscles, 86, 94
end bulbs, 261
glands, 235
Kupfer's vacuoles, 114

Labia glenoidalia, 60, 184
majora, 176, 177
minora, 176
Labyrinth, 241, 244, 245
Lacrimal glands, 236
arteries, 236
cells, 236
nerves, 237
Lacrimal passages, 237
erectile tissue, 237
Lactalbumin, 262
Lactase, 111
Lactation, 262
Lactoglobulin, 262
Lactose, 262
Lacunæ, 64
Lamellæ, 63
basis, 64
Haversian, 64
interposed, 64
interstitial, 64
Lamina cribrosa, 221
vitrea, 168
Langerhans' islands, 117, 118
Lanthanin, 6
Larynx, 123
arteries, 125
basal membrane, 124
cartilage, 124
elastic fiber, 124
entrance, 124
epithelium, 123
glands, 124
goblet cells, 123
lymph follicles, 124
lymphatics, 125
mucous membrane, 123
muscles, 124
nerves, 125
propria, 124
submucosa, 124
veins, 125
Lattice fibers, 113
Lecithin, 37
Lemniscus, 204
Lens, 225
equator, 225
nucleus, 226
plate, 214
Lenticular capsule, 226
cone, 226
epithelium, 225
fibers, 225
fossa, 214
saccule, 214
stars, 227
vesicle, 214
Leucocytes, 67, 68
amœboid movement, 71
eosinophilic, 4, 54, 134
granular, 182
granules, 68
neutrophilic, 4, 79
Leydig's cells, 155
Lieberkuehn's crypts, 108
Ligamentum pectinatum iridis, 229
spirale, 241
Light, 11
Limbus spiralis, 242
Lime, salts, 60, 63
Limitans externa, 216
interna, 218
Limiting cell lines, 38
Linin, 6
Lipoid, 4, 158
Lipophores, 255
Lips, 84
blood vessels, 86
cutaneous portion, 84
epidermis, 84
epithelium, 84
lymphatics, 86
mucous membranous portion, 84
muscular stratum, 85
skin, 84
Liquor folliculi, 168
Lissauer's tract, 186
Littré's glands, 148
Liver, 111
cells, 114
cell trabecula, 114
lymphatics, 115
nerves, 115
tubule, 114
Lungs, 126
basal membrane, 128
epithelium, 128
glands, 128
lymphatics, 129
mucous membrane, 128
musculature, 128
nerves, 129, 130
propria, 128
Lunula, 258
Lutein, 169
Lymph, 79
sinus, 80, 81
Lymphatic follicles, 80
glands, 80
nodules, 80
Lymphatics, 78, 79
blood vessels, 80
capillaries, 79
Lymphatics, larger, 80
roots, 79
small, 79
valves, 80
Lymphoblasts, 69, 70, 72
Lymphocytes, 4, 5, 69, 79, 82, 125
eosinophilic, 69
mast cells, 70
monophyletic, 70
neutrophilic, 69
polyphyletic, 70
transition form, 69
Lymphoid cords, 81
organs, 80

Macrophagi, 71, 72, 82, 107
Macula acustica, 239
lutea, 215, 219
neglecta, 239
Male sexual organs, 152
Malpighian corpuscle, 83, 140
Maltase, 111
Mantle fibers, 13
Marginal areola, 44
Marrow, 182
Massa intermedia, 161
Media, 74, 75
Mediastinum testis, 153
Medulla, 81
Medullary fasciculi, 81
rays, 141
sheath, 45, 46
Meibomian glands, 234
Meisner's corpuscles, 261
plexus, 110
Melanin, 254
Membrana basilaris, 242
propria, 85
reticularis, 244
tectoria, 244
vasculosa lentis, 226
Membrane, basal, 85
Mammary gland, 262
arteries, 263
cells, 263
epithelium, 263
fibers, 264
lobe, 262
lymphatics, 263
muscles, 264
nerves, 263, 264
veins, 263
Menisci, 184
Menopause, 168, 173
Menstrual period, 173
Menstruation, 168, 173
Merkel's tactile discs, 260
Mesamœboids, ichthyoid stage, 66
primitive, 66
sauroid stage, 66
Mesenchyma, 49, 214, 224, 252
Mesentery, 57, 120
Mesoderm, 178
Mesotendon, 181
Metabolism, 8
Metachromasia, 54
Metaphase, 12, 13
Meynert's decussation, 204

Microphagi, 72
Microscopic anatomy of organs, 66
Microsomes, 3, 30
Midbrain, 197, 203
Milk, 262
  ducts, 262
  emulsion, 262
  globules, 262
  plasma, 262
  ridge, 262
  saccule, 263
  stripe, 262
Mitochondria, 2, 8, 59, 162
Mitochondrial sheath, 161
Mitosis, 11
  barrel stage, 14
Moll's glands, 234, 259
Monakow's bundle, 204
Monaster, 13
Montgomery's glands, 264
Moss fibers, 202
Mother star, 13
Motor end plate, 179
  nerve fiber, 179
Mouth, mucous membrane
Movement, organs of, 178
Mucus, 4
Mueller's cells, 218
  duct, 152, 170, 171
  fibers, 218
  muscle, 223
Muscle, animal, 32
  cardiac, 38
  columns, 35
  heart, 32
  involuntary, 32
  orbicular, 234
  organic, 32
  red, 37
  smooth, 32
  spindle, 179
  striated, 32
  voluntary, 32
Muscles, 178
  arteries, 179
  fasciæ, 178
  lymphatics, 179
  nerves, 179
  veins, 179
Muscular bundles, 179
  compartment, 35
  fibers, 178
  network, 34, 38
  stratum, 84
  tissue, 32
Myelin, 46
Myeloblasts, 70, 72, 182
Myelocytes, 72
Myoblasts, 178
Myocardium, 77
Myofibrils, 178
Myometrium, 172
Myosepta, 178
Myotomes, 178

Nail, 257
  bed, 257
  field, 257
  fold, 257
Nail substance, 257
Nasal cavity, 121
  basal membrane, 122
  blood vessels, 122
  cement edges, 122
  connective tissue corium, 121
  epithelium, 121
  erectile tissue, 122
  glands, 122
  goblet cells, 122
  lymph follicles, 122
  lymphatics, 122
  mucous membrane, 121, 123
  nerves, 122
  olfactory region, 121
  papillæ, 121
  respiratory region, 121
  vestibule, 121
Nasolacrimal groove, 237
Naso-pharynx, 99
Neoplasms, 4
  syphilitic, 4
  tuberculous, 4
Nerve cell, 41
  cranial, 46
  ends, 46
  fiber, 40, 45, 46
  medulla, 46
  nucleus, 45
  olfactory, 46
  origins, 46
  spinal, 46
  structure, 42
Nervi nervorum, 213
Nervous system, 46
    arteries, 211
    blood vessels, 211
    membranes, 210
    nerves, 211
    organs of, 185
    plate, 214
    sympathetic, 46
    veins, 211
  tissue, 39
    development of, 48
Neumann's sheath, 89
Neural canal, 185
  crest, 185
  groove, 185
Neurilemma, 47
Neurites, 39
Neuroblasts, 48, 215
Neuroepithelium, 216
Neurofibrils, 39, 42, 46
Neuroglia, 47, 190
Neurokeratin, 46
Neuron, 41
Nicol prism, 34
Nipple, 262
  skin of areola, 263
Nissl's clods, 44
  granules, 44
Noduli, 78
Normoblasts, 71
Nuclear fluid, 6
Nuclei, resting, 14
Nuclein base, 5
Nucleolus, 5, 45
Nucleus, 59
  accessory, 7
Nucleus, direct division of, 11
  indirect division of, 11
  gelatinous, 184
  globosus, 203
  pulposus, 184
  red, 204
  tecti, 203
  trochlearis, 203
Nuel's space, 243

Ocular cleft, 214
  muscles, 237
    fibers, 237
    nerves, 238
Oculomotor nerve, 203
Odontoblast, 87, 90
Œsophagus, 100
  blood vessels, 101
  branches, 101
  fibrous membrane, 101
  glands, 100
  lymph follicles, 101
  lymphatics, 101
  propria, 100
  mucous membrane, 100
  muscularis mucosæ, 100
Olfactory bulb, 209, 250
  cells, 209, 249
  epithelium, 249
  fibers, 209, 249
  fossa, 249
  glands, 250
  glomerulus, 250
  hairs, 249
  lymph follicles, 249
  lymphocytes, 249
  nerve, 209, 210, 249
  organ, 249
  propria, 249
  region, 249
  vesicles, 249
Olivary body, 198
Olive, large, 198
  upper, 199
Omentum, 57
Oocytes, 165, 166, 167
Oogonia, 165
Optic artery, 221
  connective tissue, 220
  depression, 214
  fibers, 205, 220
  glia, 220
  nerve, 204, 210, 220
  pedicle, 214, 220
  tract, 204
  vein, 221
  vesicle, 214
Ora serrata, 215
Orbicularis ciliaris, 223
Ossein, 64
Ossification, 62
  directing trabeculæ, 62
  endochondrial, 62
  perichondrial, 62
Osteoblasts, 61
Osteoclasts, 4, 62
Otoliths, 240
Ovarian interstitial gland, 166
  vessel, 165

Ovary, 165
arteries, 169
cortex, 166
epithelial cells, 165
germinal cells, 165
germinal rudiment, 165
lymphatics, 169
medulla, 166
medullary substance, 165
nerves, 169
Oviduct, 170
Ovulation, 168
Ovum, 167
Oxygen, 9

Pacchionian bodies, 210
Palate, 94
blood vessels, 95
hard, 94
lymphatics, 95
mucous glands, 94, 95
mucous membrane, 94
muscular layer, 94
nerves, 95
soft, 94
Pancreas, 116
accessory nucleus, 118
arteries, 119
basal filaments, 118
centroacinar cells, 117
connective tissue capsule, 117
end pieces, 117
interlobular ducts, 117
intermediate pieces, 117
lymphatics, 119
mucous gland, 117
mucous membrane, 117
muscularis, 117
nerves, 119
propria, 117
secretion, 117
secretory capillaries, 118
secretory cells, 117
simple cylindrical epithelium, 117
Pancreatic juice, 117
Panethian cell, 108
Panniculus adiposus, 108
Papilla, 219
spiralis, 241
Papillæ, 85
circumvallate, 91
filiform, 91
foliate, 92
fungiform, 91
renal, 137
Papillary ducts, 137, 138
Papillomacular bundle, 221
Paraganglion intercaroticum, 151
Paraplasm, 3
Parathyroid, 132
blood vessels, 133
glands, 132
nerves, 133
parenchyma, 132
Parenchyma, 81, 132
Paroophoron, 170
Parotid duct, 98
Parotid gland, 98
nerves, 98
Pars cæca retinæ, 215, 222
ciliaris retinæ, 220, 231
optica, 215
Penicilli, 83
Penis, 162
fascia, 163
lymphatics, 164
nerves, 164
veins, 164
Perceptive apparatus, 214
Percipient elements, 216
Perforatorium, 160
Perichondrium, 60
Perichoroidal spaces, 222
Periderm, 252
Perilymph, 245
Perimetrium, 172
Perimysium externum, 178
internum, 178
Perineural sheath, 213
Perinuclear ring, 44
Periodental membrane, 88, 90
Periodontium, 181
Periostium, 181
Peripheral blood vessels, 213
lymphatics, 213
nerve fibers, 213
nerves, 212
Peritenorium, 180
Peritoneum, 105, 119, 130, 171
basal membrane, 120
epithelium, 119
nerves, 120
phagocytic properties, 120
propria, 120
subserosa, 120
vessels, 120
Perspiration, 259
Peyer's patches, 108
Phagocytes, 54, 72
Phalangeal process, 243
Pharynx, 99
glands, 99
hypophysis, 99
lymphatics, 99
muscular coat, 99
nerves, 99
tunica adventitia, 99
Pia mater, 210
Pigment, 44
epithelium, 215
Pillars, 242
Pinna, 248
Pituitary gland, 205
Pituitrin, 206
Plasma, 79
Plasmodesmi, 252
Plasmosomes, 3, 59
Pleochroism, 63
Pleura, 129, 130
Plexus choroidei, 211
fundamentalis, 76
intramuscularis, 76
perimuscularis, 76
Plica semilunaris, 107, 235
Polar field, 12
spindle fibers, 13
Pons *Varolii*, 201
Portio vaginalis uteri, 172
Postmenstrual period, 173
Predentine, 87
Premenstrual period, 173
Prepuce, 162
of clitoris, 176
Prespermatids, 154
Primary bundle, 180
Primitive segment columns, 136
Primordial skeleton, 58
Processus reticularis, 186
Prochondrial stage, 57
Pronephros, 136
Prophase, 12
Propria, 85
Prostate, 157
Protochondrial stage, 58
Protoplasm, 2
granular, 3
Proximal layer, 214
Pulp, 87, 88, 90
cavity, 87, 88, 90
Pupillary membrane, 224
Purkinje's cells, 202
fibers, 39
threads, 78

Radii lentis, 226
Ranvier's cross, 47
nodes, 46
rings, 46
Rathki's pouch, 205
Receptory end organs, 180
Reducing segmentation, 154
Reissner's crusta, 241
membrane, 241
Remak's fibers, 46
Renal capsule, 142
column, 141
labyrinth, 141
lobules, 141
pyramids, 141
tubules, 141
Rennin, 103, 117
Respiration, 9
Respiratory organs, 121
Rete *Malpighii*, 253
ovarii, 166
testis, 153, 155
Reteblast, 152, 165
Reticular apparatus, 7, 44
cartilage, 58
Retina, 24, 214
central area, 215
distal layer, 215
pigment, 215
proximal layer, 215
Retinacula, 255
Retzius' body, 243
Rhodopsin, 216
Riolan's muscle, 234
Rod bipolar, 217
ellipsoid, 216
fiber, 217
granule, 217
optic cell, 217
Rods, 216
Root canal, 87, 88, 90
Ruffin corpuscle, 94

Sacculus, 239
Saccus endolymphaticus, 245
Saliva, 95
Salivary corpuscles, 95
  glands, 95
  tubules, 96
Sarcolemma, 33, 37, 39
Sarcoplasm, 32, 33, 36, 38
Scala tympani, 240
  vestibuli, 240
Schizaxons, 188
Schlemm's canal, 229, 232
Schultz's comma, 192
Schwann's sheath, 45, 47, 196, 221.
Schweger's striæ, 89
Sclera, 229
  cells, 229
  connective tissue, 229
  fibers, 229
Scleral protuberance, 229
  sulcus, 229
Scrotum, 162
Sebaceous alveoli, 259
  epithelium, 259
  glands, 259
Sebum palpebrale, 234
Secretion granules, 171
Semen, 159
  formation, 154
Seminal vesicles, 157
Semilunar valves, 78
Sense of feeling, 252
  organs, 214
Sensory nerve fibers, 179
Septa, 81
Septula testis, 153
Septum longitudinare posterius, 185
  membranaceum, 77
  paramedianum, 185
  penis, 163
  urorectale, 145
Serosa, 173
Sertoli's cells, 154
Sharpey's fibers, 63, 89, 181
Sheath, adventitial, 73
  limiting, 64
  Schwann's, 45, 47, 196, 211
Sinus urogenitalis, 145
Skin, 252
  blood vessels, 260
  cells, 253, 254
  connective tissue, 255
  covering layer, 252
  epithelium, 252
  fat, 255
  fibers, 252, 254
  germinal layer, 252
  horny layer, 253
  intercellular spaces, 253
  lamellæ, 254
  lymphatics, 260
  muscles, 254
  nerves, 260
  papillæ, 253
  pigment, 254
  subcutaneous tissue, 255
Soleplate, 179
Solitary follicle, 80
Sperm, 159
  crystals, 159
Spermatic duct, 156
Spermatids, 154
Spermatocytes, 154
Spermatogenesis, 154
Spermatogonia, 154
Spermatozoa, 24, 155, 159
Sphincter iridis, 224
  papillæ, 144
  vesicæ, 146
Spinal anterior column, 186
    horn, 186
    roots, 186, 192
  blood vessels, 194
  brain portion, 185
  central canal, 185
  cord, 39, 185
  ependymal layer, 185
  ganglion, 195
  glia capsule, 185
  gray matter, 185, 188
  lateral column, 186
    horn, 186
  lymphatics, 195
  mantle layer, 185
  marginal fibers, 185
  nerve, 196
  neuroglia, 193
  posterior column, 186
    horn, 186
    roots, 186, 192
Spiral thread, 161, 162
Spleen, 82
  arteries, 83
  capsule, 82
  nerves, 83
Splenic pulp, 82
Splenocytes, 83
Spongioblasts, 48
S-shaped band, 227
Stairs, 38
Steapsin, 103, 117
Stellulæ *Verheynii,* 143
Stomach, 101
  arteries, 105
  folds, 102
  lymphatics, 105
  mother cells, 102
  nerves, 105
  parietal cells, 102
  propria, 102
  veins, 105
Stratum cinereum, 204
  corneum, 253, 254, 258
  cylindricum, 253
  germinativum, 253, 258
  granulosum, 253
  intermedium, 252
  intimum, 183
  lucidum, 254
  opticum, 204
  papillare, 254
  reticulare, 254
  spinosum, 253
  submucosum, 173
  subserosum, 173
  supravasculare, 173
  terminale, 186
  vasculare, 173
Stratum zonale, 186, 198, 204
Stria vascularis, 241
Striæ medullares, 199
  of *Retzius,* 89
Stroma, 68, 166
Subdural space, 210
Submaxillary blood vessels, 97
  excretory duct, 96
  gland, 96
  lymphatics, 97
  nerves, 97
Substantia gelatina *Rolandi,* 186, 188
Sulcus coronarius, 63
  spiralis externus, 241, 242
    internus, 242
  transversus, 239
Suprarenal adrenal, 149
  arteries, 153
  capsules, 149
  cellular cords, 150
  epithelial cortex, 149
  internal organ, 149
  lymphatics, 150
  medulla, 150
  nerve cells, 149
  nerves, 151
  septa, 149
  solid cellular cords, 149
Sweat, 259
  glands, 258, 259
  pore, 258
Sympathetic afferent fibers, 212
  ganglion, 211
  motor cells, 212
  nerve, 76
  nerve cells, 212
  sensory, 212
Synarthroses, 184
Synchondrosis, 184
Synctium, 19, 119
Syndesmoses, 184
Synovia, 183
Synovial membrane, 183

Tænia, 109
Tarsus, 234
Taste, organ of, 250
  buds, 92, 124, 250
  cells, 251
  fibers, 251
  germinal spaces, 251
  nerves, 251
  pore, 250
  rod, 251
Tavara's nodes, 78
Tears, 236
Teeth, 86
Telæ choroideæ, 211
Tendon, 56, 180
  blood supply, 180
  corpuscles, 56, 180
  fibers, 180
  lymphatics, 180
  sensory nerves, 180
  sheath, 181
  spindles, 180
Tenon's space, 229
Tensor choroideæ, 223

Terminal chambers, 85
nodule, 217
Testicle, 152
arteries, 155
ejaculatory ducts, 157
epididymis, 156
epithelium, 154
excretory passages, 156
genital ridge, 152
rudiment, 152
germinal cells, 152
cords, 152, 153
epithelium, 152
intermediate cells, 155
interstitial glands, 155
lymphatics, 155
nerves, 155
sexual rudiment, 152
veins, 155
Thalamus opticus, 205
Theca externa, 168
folliculi, 166, 167
interna, 168
Thecal lutein cells, 168
Thoracic duct, 80
Thrombogen, 71
Thymus, 133
arteries, 134
cells, 133
lymphatics, 135
nerves, 135
parenchyma, 133
physiology, 134
veins, 135
Thyroglobulin, 131
Thyroid gland, 131
arteries, 132
follicles, 131
lymphatics, 132
nerves, 132
veins, 132
Tigroid substance, 44
Tissue, 16
absorption, 18
adenoid, 51
basal corpuscle, 17
base, 17
bristle band, 18
cartilaginous, 50, 57
chordal, 49, 50
cilia, 17
collagenous, 74
connective 50, 52, 74
capsule, 80, 95, 132
corium, 84
fibrillary, 52
loose, 56, 129
submucous, 85
tight, 56
yellow, 57
cuticular band, 17
elastic, 56, 74
epithelial, 17
excretion, 17
fat, 57
flagellated cell, 17
free surface, 17
gelatinous, 49, 51
glands, 17
hair cells, 17
Tissue, lymphoid, 151
membrane, 17
metanephrogenous, 136
mucinogen granules, 18
mucus, 18
muscular, 32, 75
muscular striated, 33
nervous, 39
neuroglia, 50, 52
osseous, 50, 61
pigment, 57
protection, 17
reticular, 51
reticulated, 180
rod band, 18
root of cilia, 17
secretion, 17, 18
subcutaneous, 84
subendocardial, 77
subepicardial, 78
subpericardial, 78
subpleural, 130
supporting, 49
adenoid, 50
reticulated, 50
vesicular, 49, 50, 77
vitreous, 49, 51
Tomes' fiber, 90
granular layer, 88
process, 87
Tongue, 91
arteries, 93
ganglia, 94
lymphatics, 93
mucous membrane, 91
musculature, 91, 93
nerve supply, 93
submucosa, 91
veins, 93
Tonsil, 95
pharyngeal, 99
tube, 99
Tooth band, 86
crown, 88
rudiment of permanent, 88
Trabecula, 81, 82
Trachea, 125
arteries, 125
cartilaginous rings, 125
epithelium, 125
glands, 125
lymphatics, 125
mucous membrane, 125
musculature, 125
nerves, 125
propria, 125
submucosa, 125
Tractus acustico-tectalis, 204
cerebelli tegmentalis mesencephali, 203
fastigio-bulbaris, 203
olivo-cerebellaris, 198
rubro-spinalis, 204
solitarius, 198
tecto-spinalis, 204
vestibulo-cerebellaris, 199
vestibulo-spinalis, 199
Transition portion, 84
Trigeminus, 200
Trigona fibrosa, 77
Trypsin, 117
Tubal canal, 245
Tuberculi contorti, 153
recti, 153, 155
Tuberculum acusticum, 199
Tubotympanal canal, 245
Tunica adventitia, 73
albuginea, 153, 166
dartos, 163
intima, 73
media, 73
propria, 84
submucosa, 85
vaginalis propria, 153
Tympanal cover layer, 242
wall, 242
Tympanum, 245

Urea, 113, 138
Ureter, 136, 137, 144
Ureteral sheath, 144
Urethra, 146
cloaca, 146
female, 148
male, 147, 162
primary, 146
Uric acid, 138
Urinary bladder, 145
organ, 136
Urine, 138
Urogenital sinus, 162, 172
Uterine glands, 172
Uterovaginal canal, 170, 171
Uterus, 17
arteries, 174
lymphatics, 174
membrana propria, 172
mucous membrane, 172
muscularis, 172
nerves, 174
peritoneal coat, 172
smooth muscle fiber, 172
Utriculus, 239
prostaticus, 158

Vacuoles, 59
Vagina, 174
adventitia, 175
arteries, 175
flat epithelium, 175
lymphatics, 175
mucous membrane, 175
muscularis, 175
nerves, 175
propria, 175
submucosa, 175
veins, 175
vestibule, 176
Valvulæ conniventes, 106
Vas afferens, 142
deferens, 156
efferens, 82, 142
spirale, 242
Vasa hyaloidea, 230
vasorum, 76
Vascular system, 66
Vasoglossopharyngeal nerve, 198
nucleus, 198

Vater-Pacini's corpuscles, 86, 94, 261
Veins, 75
  adventitia, 75
  connective tissue, 75
  media, 75
  muscular tissue, 75
  valves, 75
Venæ corticales, 143
  rectæ, 143
  stellatæ, 143
Venulæ rectæ, 143
Venulæ rectæ corticales, 143
Vermiform appendix, 108
Vessel, central chyle, 107
  lacteal, 107
Villi, 106, 107
Villous epithelium, 107
Visual center, 205
Visual purple, 216
  tract, 204
Vitelli of embryonal cells, 4
Vitreous, 230
  anterior, 227
  fibrils, 230
  fluid, 230
  humor, 51
  membrane, 168
  tissue, 230
Vocal cords, 124
  false, 124
  true, 124
Vortex lentis, 226

Wandering cells, 52
Westphal-Edinger nuclei, 203
Wharton jelly, 51
White matter, 190
  nerve fibers, 190
Wolffian body, 136, 153
  duct, 136, 146, 153, 166
Wrisbergi portio intermedia, 200

Yolk globules, 167, 168

Zona fasciculata, 149
  glomerulosa, 149
  parenchymatosa, 166
  pellucida, 167
  reticularis, 149
  vasculosa, 166
Zonula ciliaris, 230
  cells, 231
  fibers, 230
Zonule of *Zinn*, 230

3.H.167.
A textbook of histology. Tr. fr1915
Countway Library AHI0089
3 2044 045 089 174

3.H.167.
A textbook of histology. Tr. fr1915
Countway Library AHI0089
3 2044 045 089 174